In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 27, 2023

MARIA AMBRIZ, *as representative, of Estate of Stephanie Delapaz*,	*	No. 15-502V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Decision on Entitlement; Human Papillomavirus ("HPV") Vaccine; Autoimmune Autonomic Ganglionopathy ("AAG")
Respondent.	*	

Sean F. Greenwood, The Greenwood Law Firm, Houston, TX, for Petitioner.
Steven Santayana, United States Department of Justice, Washington, DC, for Respondent.

DECISION ON ENTITLEMENT[1]

On May 15, 2015, Stephanie Delapaz filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program.[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). Ms. Delapaz alleged that the human papillomavirus ("HPV" or "Gardasil") vaccine she received on May 15, 2012, caused her to suffer from "autonomic neurocardiogenic syncope with dysautonomia"[3] and "migraine-like headaches." Pet. at 7. Following the unexpected and non-

[1] This Decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

[3] The autonomic nervous system is "the portion of the nervous system concerned with regulation of the activity of cardiac muscle, smooth muscle, and glandular epithelium[.]" *Dorland's Illustrated Medical Dictionary* 1829 (33rd ed. 2020) [hereinafter "*Dorland's*"]. It is "usually restricted to the two visceral efferent peripheral components, the sympathetic nervous system, and the parasympathetic nervous system." *Id.* The sympathetic nervous system is "the portion of the autonomic nervous system that receives its fibers of connection with the central nervous system through the thoracolumbar outflow of visceral efferent fibers." *Id.* at 1834. The parasympathetic nervous system is "the craniosacral division of the autonomic nervous system, its preganglionic fibers traveling with cranial nerves III, VII, IX, and X, and with the second to fourth sacral ventral roots; it innervates the heart, the smooth muscle and glands of

vaccine related death of Ms. Delapaz, on October 12, 2021, I granted Maria Ambriz's ("Petitioner") motion to change the caption and continue the prosecution of this case on behalf of her daughter. ECF No. 101. Petitioner modified the claim in her prehearing briefing to allege that the May 15, 2012 HPV vaccine caused Ms. Delapaz to suffer autoimmune autonomic ganglionopathy[4] ("AAG"). ECF No. 108.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[5] I find that Petitioner has failed to provide preponderant evidence that the HPV vaccine Ms. Delapaz received on May 15, 2012, was the cause-in-fact of her alleged AAG. Accordingly, Petitioner is not entitled to compensation.

I. Procedural History

On May 15, 2015, Ms. Delapaz filed a petition for compensation. Pet. Ms. Delapaz attached an affidavit to her petition. Pet'r's Ex. 1, ECF No. 1.[6] Ms. Delapaz filed medical records on a compact disc on June 30, 2015. Pet'r's Exs. 2–14; *See* ECF No. 8. Ms. Delapaz filed additional medical records on September 9, 2015. Pet'r's Ex. 15, ECF No. 10-1; Pet'r's Ex. 17, ECF No. 11-1. Ms. Delapaz filed a status report stating that she was working to obtain outstanding medical records on October 30, 2015, and the presiding special master held a status conference on that date. ECF No. 12; Min. Entry, docketed Oct. 30, 2015. Ms. Delapaz filed outstanding medical records on a compact disc on December 22, 2015. Pet'r's Exs. 19–22; *see* ECF No. 19. The presiding special master held a status conference on January 4, 2016, and ordered Ms. Delapaz to file her remaining medical records. Min. Entry, docketed Jan. 4, 2016; Sched. Order, ECF No. 20. Ms. Delapaz filed medical records on a compact disc on March 3, 2016, and a statement of completion the next day. Pet'r's Ex. 23; ECF Nos. 23–24. Following a status conference held on March 21, 2016, the presiding special master issued orders allowing Ms. Delapaz to serve subpoenas to some of her providers for the purpose of obtaining outstanding records. Min. Entry, docketed March 21, 2016; ECF Nos. 26–28. Ms. Delapaz filed a medical record on April 26, 2016. Pet'r's Ex. 24, ECF No. 29-1. She filed an additional medical record on a compact disc on May 10, 2016. Pet'r's Ex. 25; ECF No. 34.

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the head and neck, and the thoracic, abdominal., and pelvic viscera." *Id.* at 1832. Neurocardiogenic syncope is a neurally mediated syncope, which is "a serious type of vasovagal syncope precipitated by a stimulus that causes either bradycardia, or a decrease in vascular tone, or both at once." *Id.* at 1788. Vasovagal syncope, or vasodepressor syncope, is "a transient vascular and neurogenic reaction marked by pallor, nausea, sweating, bradycardia, and rapid fall in arterial blood pressure, which, when below a critical level, results in loss of consciousness and characteristic electroencephalographic changes." Dysautonomia is "malfunction of the autonomic nervous system." *Id.* at 569.

[4] Ganglion is "anatomic terminology for a group of nerve cell bodies located outside the central nervous system[.]" *Dorland's* at 751.

[5] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

[6] The affidavit begins on the ninth page of ECF No. 1.

The presiding special master held a status conference on May 25, 2016. Min. Entry, docketed May 25, 2016. Ms. Delapaz filed a status report as well as a summary opinion from Dr. Svetlana Blitshteyn and a medical record chronology on June 23, 2016. Pet'r's Exs. A–B, ECF No. 36. Ms. Delapaz filed an additional medical record on July 5, 2016, and a supplemental affidavit the next day. Pet'r's Ex. 26, ECF No. 37-1; ECF No. 39-1.[7] Ms. Delapaz filed medical records on compact discs on August 4 and 10, 2016. Pet'r's Exs. 27–28; ECF Nos. 42, 44. She also filed a statement of completion on August 10, 2016. ECF No. 45. Following an August 23, 2016 status conference, Ms. Delapaz filed an additional medical record on a compact disc on August 24, 2016. Min. Entry, docketed Aug. 23, 2016; Pet'r's Ex. 29; ECF No. 47. She submitted an expert report from Dr. Blitshteyn and medical literature on October 18 and 19, 2016. *See* Pet'r's Ex. 28 (hereinafter "Pet'r's Ex. 28(a)"), ECF No. 111-1;[8] Pet'r's Exs. 29–49, ECF No. 50.

On February 3, 2017, Respondent filed his Rule 4(c) report, arguing that this case was not appropriate for compensation. Resp't's Report at 2, ECF No. 54. Respondent also filed an expert report from Dr. Phillip Low and medical literature on this date. Resp't's Exs. A–M, ECF Nos. 55–56. Ms. Delapaz filed a supplemental expert report from Dr. Blitshteyn and additional medical literature in March of 2017. Pet'r's Ex. 50, ECF No. 58-1; Pet'r's Exs. 51–52, ECF No. 59; Pet'r's Exs. 53–55, ECF No. 62; Pet'r's Ex. 56, ECF No. 63-1.[9] The presiding special master held a status conference on March 27, 2017. Min. Entry, docketed Mar. 27, 2017. Ms. Delapaz filed affidavits from herself and Petitioner regarding Ms. Delapaz's symptoms on May 23, 2017. Pet'r's Exs. 57–58,[10] ECF No. 65. Respondent submitted a supplemental report from Dr. Low, along with medical literature, on May 26, 2017. Resp't's Exs. O–P, ECF No. 67.

On June 26, 2017, the presiding special master set an entitlement hearing for September 26–27, 2018. ECF No. 69 at 1. Ms. Delapaz filed a motion for interim attorneys' fees and costs on July 27, 2017, and Respondent did not object. ECF Nos. 71–72. The presiding special master deemed an award of interim fees and costs appropriate and awarded the full amount requested on August 31, 2017. ECF No. 73.

This case was reassigned to me on January 16, 2018. ECF Nos. 77–78. On June 25, 2018, Ms. Delapaz communicated that Dr. Blitshteyn had become unable to testify on the scheduled hearing dates. ECF No. 80. Because the parties were unable to find mutually agreeable alternative hearing dates in 2018 or 2019, the hearing was canceled. *See* ECF Nos. 81–85. On August 21, 2019, I rescheduled the entitlement hearing for September 22–23, 2020. ECF No. 87. The hearing

[7] Ms. Delapaz's supplemental affidavit did not include an exhibit number.

[8] This exhibit was originally filed as ECF No. 49, but it was refiled because it was not marked as an exhibit or Bates stamped. Petitioner also filed the report on November 18, 2016, as Petitioner's Exhibit 50. *See* ECF No. 52-1. Because Petitioner later filed a different supplemental report as Exhibit 50, I will refer to Petitioner's first formal expert report as Petitioner's Exhibit 28(a).

[9] Ms. Delapaz filed a status report on March 31, 2017, stating that one piece of medical literature Dr. Blitshteyn cited in her latest expert report was pending publication and currently unavailable. ECF No. 64 at 1. At that time, Ms. Delapaz stated that she would file the article when it became available. *Id.*

[10] The presiding special master issued an order on May 24, 2017, noting that both affidavits were marked as Exhibit 57. Order, ECF No. 66. The presiding special master stated that she would refer to Ms. Delapaz's affidavit as Exhibit 57 and to Petitioner's affidavit as Exhibit 58. *Id.*

was canceled on June 26, 2020, due to delays caused by the COVID-19 pandemic. *See* Hearing Order, docketed June 26, 2020. On September 21, 2020, I rescheduled the entitlement hearing for April 14–15, 2021. ECF No. 90.

On November 3, 2020, Petitioner's counsel filed a notice of Ms. Delapaz's death. ECF No. 91. Petitioner's counsel indicated that Ms. Delapaz's family wished to proceed with this case and that counsel would notify Chambers when an administrator was appointed. Informal Comm., docketed Nov. 18, 2020. On March 23, 2021, I held a status conference in this case. Min. Entry, docketed Mar. 23, 2021. Petitioner's counsel explained the circumstances making it difficult to establish an administrator prior to the entitlement hearing. Order, ECF No. 93. I canceled the entitlement hearing due to the extenuating circumstances. *Id.*

On July 1, 2021, Petitioner's counsel filed a status report on Ms. Delapaz's behalf indicating the status of the probate proceedings. ECF No. 94. Petitioner's counsel filed Petitioner's motion for interim fees and costs on September 2, 2021. ECF No. 95. On September 7, 2021, Petitioner's counsel filed a status report stating that Petitioner had been appointed as administrator of Ms. Delapaz's estate. ECF No. 96. Petitioner's counsel filed a copy of the Harris County, Texas probate court's order appointing Petitioner as administrator. Pet'r's Ex. 63, ECF No. 97-1. Petitioner's counsel filed a motion to amend the case caption on September 15, 2021. ECF No. 98. I granted Petitioner's motion to amend the case caption on October 12, 2021. Order, ECF No. 101.

On January 5, 2022, I scheduled an entitlement hearing for May 24–25, 2022. Hearing Order, ECF No. 104. On March 14, 2022, Petitioner filed an amended petition alleging that Ms. Delapaz suffered from Table anaphylaxis[11] as well as AAG. ECF No. 107. Petitioner filed a prehearing brief on March 18, 2022. ECF No. 108. I held a status conference with the parties on March 25, 2022, to discuss Petitioner's amended petition. Min. Entry, docketed Mar. 25, 2022; Sched. Order, ECF No. 109. On April 5, 2022, the parties filed a joint status report stating that Petitioner would not proceed with a separate anaphylaxis claim. ECF No. 112 at 1. Respondent filed a prehearing brief on April 13, 2022. ECF No. 115. He filed additional medical literature on April 18, 2022. Resp't's Exs. Q–X, ECF No. 116. I struck Petitioner's amended petition since Petitioner decided not to pursue a separate anaphylaxis claim on April 21, 2022. Order, ECF No. 117. On April 28, 2022, I issued a decision granting Petitioner's motion for interim fees and costs. ECF No. 118.

I held an entitlement hearing remotely in this case on May 24 and May 25, 2022. Min. Entry, docketed May 25, 2022. On June 7, 2022, Petitioner filed a status report stating that she did not intend to file a post-hearing brief. ECF No. 129.

This matter is now ripe for consideration.

II. Factual Background

[11] Anaphylaxis is "a type I hypersensitivity reaction in which exposure of a sensitized individual to a specific antigen or hapten results in urticaria, pruritus, and angioedema, followed by vascular collapse and shock and often accompanied by life-threatening respiratory distress." *Dorland's* at 73.

A. Medical Records

Ms. Delapaz's medical history is significant for allergies and asthma. Pet'r's Ex. 2 at 30–32. Between March 22, 1997, and May 26, 2009, she received routine childhood vaccinations, including recommended doses of tetanus, diphtheria, acellular pertussis, Haemophilus influenzae type B, Hepatitis A, and Hepatitis B vaccines. Pet'r's Ex. 21 at 1– 2. On May 4, 2011, Ms. Delapaz presented to her primary care physician's ("PCP") office due to pain in her lower chest/upper abdomen. *Id.* at 494. Ms. Delapaz complained of dizziness and headache as well as nausea and abdominal pain. *Id.* at 494–95. The assessment included unspecified constipation, polyuria,[12] polydipsia,[13] and left-sided chest wall pain. *Id.* at 496.

On May 15, 2012, Ms. Delapaz was examined by her pediatrician, Dr. Sharon Pettway, and received the HPV vaccine at issue at approximately 5:00 PM. Pet'r's Ex. 7 at 35. Later that evening, Petitioner called Dr. Pettway to report that Ms. Delapaz was experiencing chest pain, wheezing, and a headache. Pet'r's Ex. 21 at 686. On Dr. Pettway's recommendation and with concerns of an allergic reaction to the HPV vaccination, Petitioner took Ms. Delapaz to the emergency room ("ER"). *Id.*

While at the ER, Ms. Delapaz reported lightheadedness, chest burning, headache, and feeling like her heart was racing since her vaccination. Pet'r's Ex. 23 at 56. An EKG was done due to concerns about right upper arm swelling, and the results came back normal. *Id.* at 59, 63. She was diagnosed with an "[a]llergic reaction – unknown allergic reaction," and her treatment included prednisone,[14] Benadryl, Tylenol, and Zofran.[15] *Id.* at 58–59. Two days later, on May 17, 2012, Ms. Delapaz presented to her pediatrician with continued complaints consistent with an allergic reaction. *See* Pet'r's Ex. 21 at 699. Ms. Delapaz's complaints included redness along the face, hands, and feet. *Id.* Her medical history noted her recent ER visit "secondary to [an] allergic reaction to [the] HPV shot." *Id.* Ms. Delapaz was seen at the ER again the next day with continuing similar symptoms and diagnosed with an allergic reaction and unspecified chest pain. Pet'r's Ex. 23 at 38–42. Petitioner suspected that Ms. Delapaz had an allergic reaction to prednisone. *Id.* at 41. Petitioner took Ms. Delapaz to an allergist on May 25, 2012. Pet'r's Ex. 2 at 27. Ms. Delapaz reported severe allergy symptoms "in the past four weeks," with reactions to several items, including pineapple, popcorn, Gardasil, and Solumedrol.[16] *Id.*

On July 16, 2012, Ms. Delapaz was seen by her allergist and reported that she was "satisfied with her health," and had "[n]o problems with medication." *Id.* at 17. Ms. Delapaz "denie[d] chest tightness, coryza,[17] cough, dizziness, ear pain, globus sensation, headache, hoarseness, nasal

[12] Polyuria is "the passage of a large volume of urine in a given period[.]" *Dorland's* at 1472.
[13] Polydipsia is "chronic excessive thirst and intake of fluid[.]" *Dorland's* at 1466.
[14] Prednisone is "a synthetic glucocorticoid derived from cortisone, administered orally as an antiinflammatory and immunosuppressant in a wide variety of disorders." *Dorland's* at 1486.
[15] Zofran, or ondansetron, is "a serotonin receptor antagonist with antiemetic actions[.]" *Dorland's* at 1303.
[16] Solumedrol, or methylprednisolone sodium succinate, is "a synthetic glucocorticoid derived from progesterone[.]" *Dorland's* at 1137–38.
[17] Coryza is acute rhinitis. *Dorland's* at 417.

congestion, nasal drainage, nausea, pharyngitis,[18] post[-]nasal drainage, reddened eyes, reflux, sinus infections, sinus pain, sneezing, tearing or urticaria.[19]" *Id.* at 18–19.

Beginning August 7, 2012, Petitioner regularly took Ms. Delapaz to the ER and her allergist for treatment of new allergy symptoms. On August 7, 2012, Ms. Delapaz was seen in the ER with complaints of tongue swelling, shortness of breath, and hives. Pet'r's Ex. 23 at 26. Two days later, on August 9, 2012, Ms. Delapaz followed up with her allergist, and on August 10, 2012, she returned to the ER. Pet'r's Ex. 2 at 8; Pet'r's Ex. 23 at 7. Ms. Delapaz continued to complain of tongue swelling, and was also experiencing generalized chest pain, right shoulder pain, and feet swelling. Pet'r's Ex. 23 at 8. The ER physician noted that Ms. Delapaz was on prednisone, and the physician suspected leukocytosis[20] due to steroids. *Id.* at 11.

On August 12, 2012, Ms. Delapaz presented to a different children's hospital with allergic symptoms, including wheezing, nausea, vomiting, and swelling of her face, tongue, hands, and feet. Pet'r's Ex. 25 at 41. She returned the following day after a premature discharge and was admitted. *Id.* at 44. A treating resident physician stated that Ms. Delapaz was "[u]nlikely [to be experiencing an] allergic response given [the] time course of [her] illness." *Id.* at 47. The physician continued that Ms. Delapaz was "[p]ossibly [suffering from] hereditary angioedema[,][21] but [the physician] would expect more severe tongue and lip swelling, and hand and feet swelling would[not] be consistent." *Id.* The attending physician "d[id] not feel strongly that this [was] angioedema . . . ." *Id.* Ms. Delapaz returned to the same ER on August 30, 2012, with eye swelling, headache, cough, chest pain, tongue swelling, hand swelling, and an itchy throat. *Id.* at 156. Petitioner reported that Ms. Delapaz had "a longstanding history of severe allergies," with "intermittent episodes similar to this one for the past year." *Id.* Ms. Delapaz reported that she was taking Zyrtec, levalbuterol,[22] and Benadryl, and she noted that she had recently completed a course of oral steroids. *Id.* The ER physician directed Ms. Delapaz to continue her current home medications, and she prescribed Xopenex.[23] *Id.* at 162. The physician opined that there was "[l]ikely [a] strong component of anxiety[]" in Ms. Delapaz's symptoms and prescribed Lexapro.[24] *Id.*

Ms. Delapaz saw Dr. Joshua Rotenberg, a neurologist with a sleep specialty, on October 15, 2012. Pet'r's Ex. 21 at 1218. She was referred by Dr. Pettway, due to "a [four-]month history of numerous, idiopathic autonomic symptoms that seem[ed] to ebb and flow." *Id.* Dr. Rotenberg noted that Ms. Delapaz's exam was normal with symptoms that "were difficult to localize" into

[18] Pharyngitis refers to a sore throat. *Dorland's* at 1405.
[19] Urticaria is also known as hives. *Dorland's* at 1981.
[20] Leukocytosis is "a transient increase in the number of leukocytes in the blood[.]" *Dorland's* at 1015. Leukocytes are white blood cells. *Id.*
[21] Angioedema is "a vascular reaction involving the deep dermis or subcutaneous or submucosal tissues, representing localized edema caused by dilation and increased permeability of capillaries, with development of giant wheals. Urticaria is the same reaction occurring in superficial portions of the dermis." *Dorland's* at 83.
[22] Levalbuterol is "used as a bronchodilator for the treatment and prophylaxis of reversible bronchospasm in reversible obstructive airway disease[.]" *Dorland's* at 1017.
[23] Xopenex is a name for levalbuterol hydrochloride. *Dorland's* at 2057.
[24] Lexapro, or escitalopram oxalate, is "a selective serotonin reuptake inhibitor[] . . . used as an antidepressant[.]" *Dorland's* at 640.

one neurologic location. *Id.* However, he referenced Ms. Delapaz's prior motor vehicle accident[25] as a potential basis for localization of her symptoms to a cervical spine injury. *Id.* He continued that "her peripheral vascular changes could be referable to an autonomic disorder." *Id.* Dr. Rotenberg was unable to account for Ms. Delapaz's orbital swelling. *Id.* He ordered a spine MRI to rule out myelopathy,[26] labs to detect autonomic dysfunction, and an EEG. *Id.* He also ordered a sleep study to rule out sleep disordered breathing. *Id.* Dr. Rotenberg prescribed a beta blocker[27] and clonidine[28] for pain prevention and autonomic modulation. *Id.*

The sleep study revealed "[s]ignificant snoring and hypoventilation"[29] but "no significant obstructive sleep apnea[]"[30] or oxygen desaturations." *Id.* at 1225. The EEG was "normal for the patient's age and conscious state." *Id.* at 1239. The autonomic dysautonomia evaluation revealed "no informative autoantibodies[.]" *Id.* at 1255. The report cautioned, however that "a negative result does not exclude neurological autoimmunity with or without associated neoplasia."[31] *Id.* at 1255–56. Dr. Rotenberg listed anxiety, being overweight, and extrinsic asthma among the reasons he directed Ms. Delapaz to have an MRI. *Id.* at 1234. Ms. Delapaz's MRI showed normal alignment of the cervical spine, no bony edema,[32] unremarkable prevertebral soft tissue, and no ligamentous injury, canal stenosis,[33] neurocranial[34] narrowing or cord compression. *Id.* at 1235. The radiologist's impression was "unremarkable noncontrast MR cervical spine."[35] *Id.*

Following "a seizure-like episode involving [right] arm jerking and eye rolling[,]" Ms. Delapaz was admitted to Texas Children's Hospital on November 29, 2012. Pet'r's Ex. 25 at 245, 250. A brain MRI was unremarkable, and the physician noted that prior evaluations by her primary care provider, allergy and immunology, and neurology were also negative. *Id.* The discharge assessment listed "a six[-]month history of assorted symptoms including throat tightness, chest

[25] It is unclear when this accident occurred.
[26] Myelopathy is "any of various functional disturbances or pathologic changes in the spinal cord, often referring to nonspecific lesions in contrast to the inflammatory lesions of myelitis." *Dorland's* at 1203.
[27] Beta-adrenergic blocking agents induce adrenergic blockade, which is "selective inhibition of the response to the sympathetic impulses and to catecholamines and other adrenergic amines at either the alpha or beta receptor sites of the effector organ or at the postganglionic adrenergic neuron." *Dorland's* at 38, 224. Adrenergic means "activated by, characteristic of, or secreting epinephrine or related substances, particularly referring to the sympathetic nerve fibers that liberate norepinephrine at a synapse when a nerve impulse passes." *Id.* at 33.
[28] Clonidine can be used as an antihypertensive, to prevent migraine, and for other conditions. *Dorland's* at 368.
[29] Hypoventilation is "a state in which there is a reduced amount of air entering the pulmonary alveoli . . . resulting in increased carbon dioxide tension." *Dorland's* at 896.
[30] Sleep apnea is "transient periods of cessation of breathing during sleep." *Dorland's* at 115. Obstructive apnea results "from collapse or obstruction of the airway with the inhibition of muscle tone that occurs during REM sleep." *Id.*
[31] Neoplasia is "the formation of a neoplasm, i.e., the progressive multiplication of cells under conditions that would not elicit, or would cause cessation of, multiplication of normal cells." *Dorland's* at 1221.
[32] Edema is "the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to subcutaneous tissues." *Dorland's* at 587.
[33] Stenosis is "an abnormal narrowing of a duct or canal[.]" *Dorland's* at 1740.
[34] The neurocranium is "the portion of the cranium that encloses the brain[.]" *Dorland's* at 1246.
[35] The cervical spine consists of "the upper seven vertebrae, constituting the skeleton of the neck." *Dorland's* at 1720, 2020.

pain, eye/hand/foot swelling, hand/foot color changes, and episodes of being difficult to arouse and finding herself on the ground without explanation." *Id.* at 250. There was a "[q]uestion of hypoglycemia prior to admission, [but] all [blood glucose readings were] normal" while admitted. *Id.* Discharge diagnoses included syncope and collapse, unspecified anxiety, unspecified hypoglycemia, unspecified extrinsic asthma, and unspecific obesity. *Id.* at 241. The treating physician recommended follow-ups with neurology and psychiatry. *Id.* at 250. Conversion disorder[36] is listed as a differential diagnosis. *Id.* Ms. Delapaz was discharged on December 1, 2012. *Id.* at 245.

Two weeks later, Ms. Delapaz was again admitted to Texas Children's after experiencing chest pain. *Id.* at 384–85. Her patient history included a note that a neurology exam revealed "lack of sweating and enlarged pupils." *Id.* at 385. During her hospitalization, Ms. Delapaz was seen by neurologist Dr. Melissa Jones, who noted that "[m]ultiple symptoms are concerning for autonomic dysfunction[,]" including headaches, confused episodes, tremor and seizure-like activity, and difficulty walking. Pet'r's Ex. 21 at 1287. Ms. Delapaz was discharged on December 17, 2012, with final diagnoses of "[c]hest pain/pneumomediastinum[,[37] a]nxiety[, and h]ypoglycemia/[h]yperglycemia[.]" Pet'r's Ex. 25 at 384. As of December 14, 2012, Ms. Delapaz was directed to begin taking hydrocodone/acetaminophen[38] and was continuing multiple medications, including loratadine[39] and diphenhydramine.[40] Pet'r's Ex. 19 at 42. Records from Texas Children's indicate that Ms. Delapaz's hydrocodone was discontinued on January 8, 2013. *See* Pet'r's Ex. 25 at 453.

On December 18, 2012, Ms. Delapaz was evaluated by pediatric rheumatologist Dr. Marietta de Guzman. *Id.* at 536. Dr. de Guzman determined that the "[n]ature of her historical features, complaints and unremarkable physical examination findings DID not define chronic arthritis or a systemic disorder (e.g.[,] Lupus and lupus spectrum disorders)."[41] *Id.* at 543 (emphasis in original).

Ms. Delapaz underwent further autonomic testing in December of 2012, which revealed, "[s]evere sudomotor[42] system dysfunction[]" and "[c]ardiovagal system dysfunction." Pet'r's Ex.

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[36] Conversion disorder is "a mental disorder characterized by conversion symptoms (loss or alteration of voluntary motor or sensory functioning suggesting physical illness, such as seizures, paralysis, dyskinesia, anesthesia, blindness, or aphonia) having no demonstrable physiologic basis . . . ." *Dorland's* at 542.

[37] Pneumomediastinum is "the presence of air or gas in the mediastinum, which may interfere with respiration and circulation and may lead to such conditions as pneumothorax or pneumopericardium." *Dorland's* at 1449.

[38] Hydrocodone is a semisynthetic opioid analgesic derived from codeine but having more powerful sedative and analgesic effects. *Dorland's* at 867.

[39] Loratadine is "a nonsedating antihistamine (H1 receptor antagonist) with no significant antimuscarinic effects[.]" *Dorland's* at 1060.

[40] Diphenhydramine is "a potent antihistamine (H1 receptor antagonist) with anticholinergic, antitussive, antiemetic, antivertigo, antidyskinetic, and sedative actions." *Dorland's* at 516.

[41] Lupus disorders, or lupus erythematosus, are "a group of connective tissue disorders primarily affecting women aged [twenty] to [forty] years, comprising a spectrum of clinical forms in which cutaneous disease may occur with or without systemic involvement." *Dorland's* at 1066.

[42] Sudomotor refers to "stimulating the sweat glands." *Dorland's* at 1766.

19 at 45–48. Her "[s]udomotor test [was] remarkably abnormal because of [the] absence of sweat production at all the testing locations, indicative of severe impairment or post-ganglionic, sympathetic-cholinergic[43] nerve fibers." *Id.* at 48. A ten-minute tilt test[44] showed "no significant decline in systolic or diastolic blood pressure." *Id.* at 47. The neurologist performing the testing, Dr. Harati, determined that Ms. Delapaz had a composite autonomic scoring scale ("CASS") of 6, with a sudomotor subscore of 3, a cardiovagal subscore of 3, and an adrenergic subscore of 0. *Id.* On December 22, 2012, she was scheduled to begin IVIG treatment. Pet'r's Ex. 21 at 1038.

On February 6, 2013, Ms. Delapaz was seen by a new treater, pediatric neurologist Dr. Imad Jarjour, after being referred by Dr. Pettway for an autonomic evaluation. Pet'r's Ex. 25 at 688. Ms. Delapaz reported that she "was in good health [un]til [seven] months ago when she developed random swelling in her face, throat, and fatigue, without fevers, along with nausea." *Id.* Ms. Delapaz also noted experiencing purple hands and feet, white spots on skin, mild chest pain, anxiety, fatigue, confusion, postural dizziness, vasovagal fainting, mild hand tremors, arthralgias,[45] and intermittent hypertension. *Id.* Dr. Jarjour referenced Ms. Delapaz's December 2012 testing "which showed no response on sweat test, [quantitative sudomotor axon reflex test ("QSART,")] and cardio-vagal dysfunction on heart rate ratio, but no orthostatic hypotension [("OH")][46] or tachycardia[47] on tilt, and no cardio-adrenergic dysfunction on Valsalva[48] blood pressure responses." *Id.* He also noted that "[s]he was hypertensive at baseline while supine 143/94 and [had a heart rate] of 97 (she is obese)." *Id.* Ms. Delapaz's history revealed treatment "for putative immune mediated autonomic neuropathy[49] with IVIG on 12/24/2012[.]" *Id.* at 689. Ms Delapaz reported "joint pains as a side effect[] and worse headaches." *Id.* Dr. Jarjour noted that Ms. Delapaz's IVIG treatment "may have helped her recover patchy areas of sweating[]" and that she was not experiencing hypertension, confusion, dry mouth, joint swelling, rash, chest pains, or meningeal signs post IVIG treatment. *Id.*

Dr. Jarjour included an exhaustive list in his review of Ms. Delapaz's autonomic symptoms:

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[43] Cholinergic is "a term applied to the sympathetic and parasympathetic nerve fibers that liberate acetylcholine at a synapse when a nerve impulse passes." *Dorland's* at 346. Acetylcholine is "a cholinergic agonist and serves as a neurotransmitter at the myoneural junctions of striated muscles, at the autonomic effector cells innervated by parasympathetic nerves, at the preganglionic synapses of the sympathetic and parasympathetic nervous systems, and at various sites in the central nervous system." *Dorland's* at 12.

[44] A tilt table test, or tilt test, is "measurement of various bodily responses while the patient is tilted to different angles on a tilt table, usually head up, such as monitoring of circulatory, cardiac, and neurologic responses." *Dorland's* at 1872.

[45] Arthralgia is joint pain. *Dorland's* at 154.

[46] OH is "a fall in blood pressure associated with dizziness, blurred vision, and sometimes syncope, occurring upon standing or when standing motionless in a fixed position[.]" *Dorland's* at 894.

[47] Tachycardia is "excessive rapidity in the action of the heart[.]" *Dorland's* at 1838.

[48] The Valsalva test or maneuver is "forcible exhalation effort against occluded nostrils and a closed mouth causes increased pressure in the auditory tube and middle ear, so that the tympanic membrane moves outward[.] *Dorland's* at 1087.

[49] Autonomic neuropathy is "any neuropathy of the autonomic nervous system, causing symptoms such as [OH], disordered bowel, bladder, or sexual functions, or abnormal pupillary reflexes[.]" *Dorland's* at 1251.

Headaches- multiple medications ineffective
Fatigue- improving
Orthostatic lightheadedness/dizziness- mild lately
Syncope- last one 11/20/2012
Vertigo- at rest and mostly with headaches
Vasomotor symptoms discoloration- purple hands and feet at rest, better lately
Too little sweating- improving after IVIG
Dry mouth- better after IVIG
Constipation- improving
Bladder involvement- no urge to urinate
Sleep problems- frequent arousals
Pupil or vision problem- blurred vision and dilated pupils
Cognition problems- forgetfulness, improving
Tremors- improving
Numbness- hands

Id.

During exam, Ms. Delapaz's pupils "were equal and reactive to light." *Id.* at 692. Her neurologic exam was normal. *See id.* at 692–93. Dr. Jarjour assessed Ms. Delapaz "[w]ith resolving systemic illness that began with facial and mouth swelling then superimposed cholinergic autonomic neuropathy, very suggestive of [an] immune-mediated disorder." *Id.* at 693. Dr. Jarjour noted that Ms. Delapaz had "improved overtime [sic] with residual various symptoms." *Id.* Due to her adverse reactions to corticosteroids and IVIG, Dr. Jarjour did not recommend either for treatment "in the absence of confirmed autoimmune disorder and active inflammation." *Id.* His final diagnosis included peripheral autonomic neuropathy of unknown cause. *Id.* at 682, 695.

Ms. Delapaz returned to Dr. Jarjour on March 6, 2013. *Id.* at 874. She described herself as "overall better[,]" but she reported bad chest pains, joint pains, and side pain. *Id.* Petitioner believed Ms. Delapaz's symptoms had returned. *Id.* Autonomic function testing had been repeated on February 21, 2013, and revealed "only mild decreased sweating in the foot[]" but was otherwise normal. *Id.* Ms. Delapaz "had subjective symptoms with tilt. No faint or near faint, mostly head pain and pressure. Cardio-vagal and cadriodrenergic [sic] functions were normal [with] no orthostatic tachycardia or hypotension or hypertension." *Id.* Dr. Jarjour concluded that Ms. Delapaz had a "resolving systemic illness that appears to be autoimmune in nature without proof however of any autoantibodies []." *Id.* at 877. Based on her normal functioning, he "rul[ed] out any dysautonomia or significant autonomic neuropathy." *Id.* at 877–78. He saw "no reason from [an] autonomic [or] neurological stand point [sic] to give her another course of IVIG or prednisone." *Id.* at 878. Dr. Jarjour determined that deconditioning, somatic hypervigilance, and anxiety accounted for her residual symptoms, and he recommended continued therapy with her treating psychiatrist and rheumatologist. *Id.*

On April 23, 2013, Ms. Delapaz presented to a new neurologist following an ER visit for an emesis[50] episode. Pet'r's Ex. 27 at 2. The neurologist noted that Ms. Delapaz was healthy until

[50] Emesis is vomiting. *Dorland's* at 602.

she developed chest pain, numbness and tingling in her arms and legs, feelings of hot and cold, and shooting joint pain in August of 2012. *Id.* Ms. Delapaz's symptoms, according to Petitioner, had returned over the past three weeks, in a manner similar to their original presentation. *Id.* The neurologist concluded that Ms. Delapaz "present[ed] with worsening symptoms of dysautonomia." *Id.* at 4. Ms. Delapaz underwent IVIG treatment and was discharged on April 25, 2013. *Id.* at 189.

Ms. Delapaz returned to the ER on April 26, 2013, and again four days later, for nausea and headache, and abdominal pain and feet discoloration, respectively. *Id.*; Pet'r's Ex. 4 at 2–3. On May 13, 2013, she presented to pediatric neurologist Dr. Ian Butler at a dysautonomia clinic "for her probable neurocardiogenic syncope[] with dysautonomia and migraine-like headache." Pet'r's Ex. 5 at 32. During a follow-up appointment on June 4, 2013, Dr. Butler noted that Ms. Delapaz's neurocardiogenic syncope was "documented on a tilt-table testing [sic] on May 21, 2013[; h]owever, there were only relatively mild changes at that time." *Id.* at 14. Ms. Delapaz was also on propranolol,[51] a medication that Dr. Butler noted "may have had an impact on that study." *Id.* Dr. Butler indicated that Ms. Delapaz's cerebrospinal fluid ("CSF")[52] folate testing indicated that she might have a deficiency. *Id.* at 15. He reasoned that a "defect in [central nervous system ("CNS")] folate may explain a number of [Ms. Delapaz's] complaints, including impaired memory, fatigue, insomnia, and hallucinations." *Id.* Dr. Butler remained "convinced that she has dysautonomia; however, given her rather mild tilt table testing, the additional evidence regarding CNS folate deficiency becomes significant." *Id.* Petitioner and Ms. Delapaz reported that Ms. Delapaz had continuing headaches, frequent syncopal episodes, memory loss, fatigue, hallucinations associated with sleep difficulties, and periodic pupil dilation. *Id.* at 14. Dr. Butler directed Ms. Delapaz to continue propranolol and Diamox,[53] and he prescribed Florinef.[54] *Id.*

On June 14, 2013, Ms. Delapaz followed up at the dysautonomia clinic. *Id.* at 8. Dr. Butler planned "to repeat her formal tilt-table testing [] without pharmacological agents that could interfere with that study[,]" as well as repeat the CSF testing. *Id.* at 9. Dr. Butler discussed with Petitioner "the importance of having a complete and appropriate diagnosis in [Ms. Delapaz] rather than treating her symptoms without a definitive diagnosis." *Id.* He also noted that Ms. Delapaz had a recent history of aseptic meningitis[55] and hemolytic anemia[56] following her second dose of IVIG. *Id.*

Ms. Delapaz returned to the dysautonomia clinic on June 24, 2013, and she exhibited significant improvement on the propranolol. *Id.* at 1. Dr. Butler suggested a formal tilt table test in

[51] Propranolol is "a nonselective beta-adrenergic blocking agent that lacks intrinsic sympathomimetic activity, decreases cardiac rate and output, reduces blood pressure, and is effective in the prophylaxis of migraine." *Dorland's* at 1504.
[52] Cerebrospinal fluid is "the fluid contained within the four ventricles of the brain[.]" *Dorland's* at 1052.
[53] Diamox, or acetazolamide, is "a carbonic anhydrase inhibitor with a wide variety of uses[] . . . ." *Dorland's* at 12.
[54] Florinef, or fludrocortisone acetate is a "synthetic steroid with potent mineralocorticoid and high glucocorticoid activity[.]" *Dorland's* at 712.
[55] Aseptic meningitis is "any of several mild types of meningitis, most of which are caused by viruses[.]" *Dorland's* at 1117.
[56] Hemolytic anemia is "any of a group of acute or chronic anemias characterized by excessive hemolysis and impaired erythropoiesis." *Dorland's* at 78. Acquired anemias "are due to the actions of extrinsic agents such as infectious agents, poisons, physical trauma, or antibodies." *Id.*

several months following weaning from several of her medications, including steroids. *Id.* He was hopeful that fewer medications may help with her CSF levels and improve her cognitive and psychological functions. *See id.* On October 3, 2013, Ms. Delapaz presented to pediatric geneticist Dr. Erin Cooley, who also believed that her "symptoms may be attributable to excessive and unnecessary medication." Pet'r's Ex. 25 at 1267. Ms. Delapaz ultimately did not receive genetic testing due to the refusal of her insurance provider to cover the costs. *See id.* at 1342. A note from an August 19, 2014 visit to a pain specialist noted an Ehlers-Danlos syndrome[57] diagnosis in 2013. Pet'r's Ex. 26 at 1. The record also noted that Ms. Delapaz suffered from dysautonomia but that she was treated with IgG, and her dysautonomia resolved. *Id*. Ms. Delapaz continued to receive care for "chronic musculoskeletal pain due to Ehlers-Danlos syndrome" into 2015. *See id.* at 19.

B. **Affidavits & Fact Testimony**

1. Affidavits

Ms. Delapaz submitted an affidavit accompanying her petition on May 14, 2015.Pet'r's Ex. 1. She included a summary of her medical history that is consistent with her medical records. Ms. Delapaz stated that she received her HPV vaccination at Dr. Pettway's office on May 15, 2012. *Id.* at 1. Ms. Delapaz asserted that she felt weak and nauseous and had a headache following the vaccination and that Dr. Pettway told her these were normal side effects. *Id.* Ms. Delapaz stated that she presented to the ER that evening when her symptoms did not resolve, and the ER doctors concluded that she suffered from an allergic reaction to her vaccination. *Id.* at 2. Ms. Delapaz reported that she then followed up with Dr. Pettway, who advised her not to receive further HPV vaccinations. *Id.* Ms. Delapaz stated that she returned to the ER the next evening and was again treated for an allergic reaction to the HPV vaccination. *Id.* Ms. Delapaz continued that "[s]ometime around June or July 2012, [she] could not sweat[,] and [her] vision became blurry. [Her] severe headaches, nausea, and dizziness continued." *Id.* She asserted that she "began to feel fatigued and was forgetful all the time." *Id.* She noted that she could not take care of herself and needed assistance to comb her hair and shower. *Id.* Ms. Delapaz recalled her consultations with an allergist and a neurologist and stated that she presented to the emergency room multiple times during this period due to worsening and debilitating symptoms, including repeatedly falling down the stairs. *Id.* Ms. Delapaz stated that after she was referred to mental health treatment by an ER physician, she began regular treatment with a child psychiatrist and began taking Lexapro. *Id.* at 3. Ms. Delapaz asserted that her anxiety and obsessive compulsive disorder ("OCD") were "basically gone[]" as of the date of her affidavit. *Id.*

Ms. Delapaz reported that she began homebound schooling in the fall of 2012 after her symptoms caused difficulties with school. *Id.* She stated that her "vision and memory problems made schoolwork nearly impossible[]" and that she "could not concentrate or focus." *Id.* She recalled experiencing her first seizure while at a restaurant in November of 2012. *Id.*

[57] Ehlers-Danlos syndrome is "a group of inherited disorders of connective tissue[.]" *Dorland's* at 1798. "Prominent manifestations include hyperextensible skin and joints, easy bruisability, and friability of tissues with bleeding and poor wound healing, with additional symptoms specific for individual types." *Id.* at 1798–99.

Ms. Delapaz recalled beginning physical therapy to "minimize the juvenile arthritis symptoms" at the direction of Dr. de Guzman in January of 2013. *Id.* Ms. Delapaz stated that she saw her physical therapist two to three times per week until December of 2013. *Id.* Ms. Delapaz reported that her ability to sweat resumed on January 10, 2013. *Id.* She stated that her energy level improved and that she was able to take care of herself. *Id.*

Ms. Delapaz reported that her "eyes start[ed] dilating again and [her] symptoms were returning[]" in April of 2013. *Id.* She also suffered from another seizure when leaving a cardiologist's office in April of 2013. *Id.* Ms. Delapaz reported that "[b]y mid-June [of] 2013, [she] was sleeping all of the time and cried a lot because of the pain." *Id.* at 6. She stated that she "mostly stayed in bed from April to June . . ." of 2013. *Id.*

Ms. Delapaz recalled that when she was evaluated by Dr. Belmont at Texas Children's Hospital in October of 2013, he "indicated that the Gardasil shot may have caused [her] issues." *Id.* Ms. Delapaz noted that she began "natural medicine and supplements[,]" which "seemed to help[]" her symptoms, later that month. *Id.* However, Ms. Delapaz maintained that she had "severe headaches, nausea, body pains, memory issues, fainting, seizures," fatigue, and dehydration "[d]uring all of 2013[.]" *Id.*

Ms. Delapaz stated that she returned to school for half-days in 2014 and that her symptoms "substantially improved[]" that year. *Id.* She recalled that she continued experiencing pupil dilation but that her blurry vision improved. *Id.* She continued that she was not experiencing fainting or seizures and that her heart rate, blood pressure, and focus improved. *Id.* Ms. Delapaz noted that she was able to begin working part-time. *Id.* However, Ms. Delapaz stated that she had to stop working in April of 2015 because of increasing headaches and fatigue. *Id.* at 7.

Ms. Delapaz filed a supplemental affidavit on July 6, 2016. ECF No. 39-1. Ms. Delapaz stated that her symptoms had returned within the last six to eight months. *Id.* ¶ 1. She stated that she "will feel normal for a couple of days or possibly a week[,] but the symptoms always return." *Id.* Ms. Delapaz reported experiencing headaches that vary in severity but "that never go[] away." *Id.* ¶ 2. She stated that her doctors attributed her headaches to intracranial hypertension. *Id.* Ms. Delapaz noted that she never experienced intracranial hypertension until after her IVIG treatments. *Id.* Ms. Delapaz also reported blood pressure problems, memory issues, needing to sleep a lot, dehydration, and vision problems. *Id.* ¶¶ 3–7. She stated that her menstrual periods became infrequent but heavy following her vaccination and that they had since completely stopped. *Id.* ¶ 8. Ms. Delapaz recalled receiving infusions for headaches in 2015 and having two lumbar punctures that year. *Id.* ¶¶ 9–11. Ms. Delapaz indicated that her symptoms escalated between late-2015 and 2016. *See id.* ¶¶ 12–19.

Ms. Delapaz submitted a third affidavit on May 23, 2017. Pet'r's Ex. 57. Ms. Delapaz discussed her dehydration and difficulty urinating post vaccination. *Id.* ¶¶ 2–5. Ms. Delapaz stated that she "did not mention [her] issues urinating to [her] treating doctors because it did not seem like a big deal at the time. [She] was just concerned about [her] 'major' symptoms, like fainting." *Id.* ¶ 3. Petitioner also filed an affidavit on May 23, 2017. Pet'r's Ex. 58. Petitioner discussed Ms. Delapaz's difficulties with dehydration and urinating. *Id.* ¶¶ 3–5. She recalled mentioning these issues to Ms. Delapaz's treaters, but she stated that the doctors "seemed more worried about [Ms. Delapaz's] fainting and [] seizures." *Id.*

2. Hearing Testimony

Petitioner testified at the entitlement hearing on May 24, 2022. Tr. 28–74. Describing Ms. Delapaz's health prior to vaccination, Petitioner stated that "[y]ou could[not] get her to sit down." Tr. 30:11–13. Petitioner discussed Ms. Delapaz's participation in basketball and cheerleading during middle school and drill team during high school. Tr. 30:13–31:3. Petitioner also recalled Ms. Delapaz running "a lot" and participating in 5K races. Tr. 31:4–8. Petitioner described Ms. Delapaz as "happy[and] extremely active[] . . . ." Tr. 31:8. Petitioner stated that Ms. Delapaz was "completely healthy" and never experienced fainting, dizziness, or her other later symptoms before her vaccination. Tr. 31:14–17.

Petitioner asserted that she was with Ms. Delapaz "24/7[]" post vaccination. Tr. 31:18–22. Petitioner recalled that she was Ms. Delapaz's "complete caretaker because sometimes she would go kind of into a daze, and she would[not] know where she was at. She would[not] be able to communicate." Tr. 31:22–25. Petitioner recalled sleeping with her daughter on a mattress they moved downstairs due to concerns that Ms. Delapaz could fall out of their second-story window. Tr. 31:25–32:6. Petitioner stated that she never left Ms. Delapaz alone because "it was not safe for her to be alone." Tr. 32:7–12.

Petitioner stated that Ms. Delapaz received her HPV vaccination during a physical required for her to participate in drill team the upcoming school year. Tr. 32:18–20. Petitioner recalled that Ms. Delapaz "immediately [] reacted[]" after receiving the vaccine. Tr. 32:23–24. Petitioner stated that Ms. Delapaz's doctor administered a Solumedrol shot, which "actually made things worse." Tr. 33:16–18. Petitioner reported that Ms. Delapaz experienced elevated heart rate and blood pressure following her vaccination and that the Solumedrol caused Ms. Delapaz's blood pressure to increase further. Tr. 33:18–23. Petitioner recalled that Ms. Delapaz was experiencing dizziness, lightheadedness, and severe headaches. Tr. 33:23–25.

Petitioner stated that she and Ms. Delapaz returned home after staying at the doctor for more than an hour following her reaction. Tr. 34:4–6. Petitioner stated that she took Ms. Delapaz to the ER later that evening because her symptoms "calm[ed] down" and then "came back very intense[.]" Tr. 34:15–21. Petitioner discussed taking Ms. Delapaz to an allergist, who "could[not] pinpoint [the issue,] and they did[not] really believe that it was the vaccine giving an allergic reaction[. T]hey thought maybe more like the side effect or her body just could not process that type of vaccine maybe." Tr. 35:22–36:1. Petitioner recalled that Ms. Delapaz's symptoms continued to worsen and that "[t]he hospitals had no idea [why]. Every time we took her, they had no idea." Tr. 36:10–12. Petitioner testified that by the end of May of 2012, Ms. Delapaz was continuing to experience severe headaches as well as fainting, nausea, and difficulty communicating during "zombie"-like states. Tr. 36:23–37:3. Petitioner stated that Ms. Delapaz's symptoms continued to worsen through June and July of 2012. Tr. 37:4–6. Petitioner recalled doctors explaining that an allergic reaction would not continue for this long and being unsure what was causing Ms. Delapaz's symptoms. Tr. 37:7–18. Petitioner continued that Ms. Delapaz was experiencing drastic changes in blood pressure, from dangerously high to dangerously low, during this period. Tr. 37:19–38:4.

Petitioner stated that she and Ms. Delapaz noticed that Ms. Delapaz was not sweating "no matter how hot it would get[.]" Tr. 38:7–14. Petitioner testified that Ms. Delapaz stopped sweating

during the 2012 school year, within a few months of her vaccination. Tr. 38:23–39:4. Petitioner stated that Ms. Delapaz began experiencing vision problems around October of 2012. *See* Tr. 39:13–20. Petitioner recalled that she had to take Ms. Delapaz's vehicle away due to her blurry vision. Tr. 39:7–8. Petitioner reported that Ms. Delapaz frequently complained about things being "too bright[,]" and Petitioner testified that she "could tell [Ms. Delapaz's] eyes were always very dilated." Tr. 39:8–10. Petitioner recalled Ms. Delapaz experiencing a seizure at school in the fall of 2012. Tr. 39:20–40:17. Petitioner testified that in the fall of 2012, Ms. Delapaz "was starting to miss a lot of school, and . . . she would not go up and down the stairs at home. She did[not] want to take walks anymore." Tr. 40:21–23. Petitioner testified that Ms. Delapaz continued going to drill team meetings but that she was unable to participate in drill team exercises and practices. Tr. 41:2–9. Ms. Delapaz was sometimes able to participate with drill team during football games "[e]very now and then after a treatment they gave her, . . . but it would[not] last more than two or three minutes that she would actually stay on the field." Tr. 41:10–17. Petitioner stated that she was helping Ms. Delapaz to the restroom during this period and that Petitioner "would actually stand outside of the restroom[] because [Ms. Delapaz] fainted a couple of times, and" Petitioner could not hear it if she was in another area of the house. Tr. 42:1–5. Petitioner testified that Ms. Delapaz's grades began slipping due to missing school. Tr. 42:14–15. Ms. Delapaz was eventually moved to homebound schooling, but schoolwork was difficult "because her eyes were dilated, so she really could[not] see and read correctly . . . ." Tr. 42:16–21. Petitioner testified that Ms. Delapaz previously loved reading but was no longer able to . Tr. 43:1–5. Petitioner stated that they tried using bright lamps to see if they would help Ms. Delapaz read but that Ms. Delapaz was still unable to read. Tr. 43:6–10. Petitioner noted that Ms. Delapaz's grades were still down into the spring of 2013. Tr. 43:15–16. Petitioner continued that Ms. Delapaz's grades would "go back and forth, because some treatment sometimes would help her, but it created . . . two very dangerous medical conditions." Tr. 43:18–21.

Discussing Ms. Delapaz's medical treatment, Petitioner recalled that Dr. Jones "was the first [doctor] to believe everything and understand everything . . . . She did not know exactly what the problem was, but she promised that she was going to do everything she could to try to figure it out." Tr. 44:12–19. Petitioner testified that by the time Ms. Delapaz presented to Dr. Jones in October of 2012, Ms. Delapaz was experiencing dilated eyes, fainting, and staring into space. Tr. 44:24–45:1. Petitioner testified that Ms. Delapaz had tried to walk out of the house about three times when disoriented. Tr. 45:1–2. Petitioner stated that she was able to stop Ms. Delapaz from leaving the house because they were sharing a mattress downstairs, and Petitioner could feel when Ms. Delapaz left the bed. Tr. 45:2–6. Petitioner testified that Ms. Delapaz "would walk very slow. She did[not] have a lot of energy. So you did[not] hear that she was leaving unless you felt [] the movement of the bed." Tr. 45:8–11.

Petitioner discussed Ms. Delapaz's hospitalization to begin IVIG treatment in late 2012. Tr. 46–50. Petitioner recalled that Ms. Delapaz was having trouble urinating during this time. Tr. 46:20–47:13. Petitioner testified that despite "constant bags of IV fluids[,]" Ms. Delapaz went about three days without urinating while she was in the hospital. Tr. 47:8–10. Petitioner stated that Ms. Delapaz presented to Dr. Cathey and Dr. Serano at Texas Children's Hospital and that the doctors believed Ms. Delapaz had an autoimmune condition. Tr. 48:1–13. Petitioner testified that the doctors diagnosed Ms. Delapaz with "[d]ysautonomia, something autoimmune, they just did[not] know what. Autonomic system failure or a reaction, depending on which doctor said it." Tr. 48:13–15. Petitioner recalled that Ms. Delapaz's first IVIG treatment cause severe headaches and

sensitivity to light and sound. Tr. 49:2–9. Petitioner stated that Ms. Delapaz's headaches began to subside a week or two after treatment. Tr. 49:18–19. Ms. Delapaz experienced improvement in her symptoms and gradually began walking, running, visiting friends, and participating in drill team again. Tr. 49:20–50:3. Her eyes were no longer dilated, and her urination returned to normal. Tr. 50:3–5. Petitioner testified that Ms. Delapaz's improvements lasted for three to four months. Tr. 50:8–9.

Petitioner recalled that Ms. Delapaz had a second IVIG treatment, but "this time she got hemolytic anemia and aseptic meningitis. She had spinal taps and her . . . fluid levels would be really high. They had to put her on [D]iamox to bring down some of that fluid." Tr. 50:13–21. Petitioner stated that Ms. Delapaz had lumbar punctures for testing but also to remove fluid or "add a patch . . . ." Tr. 50:22–24. Petitioner testified that Ms. Delapaz's anemia and meningitis did not resolve following her second IVIG treatment and that she "was very, very close to having to have a blood transfusion." Tr. 51:5–24. Ms. Delapaz's energy levels improved somewhat after the IVIG treatment, but Petitioner stated that the steroids Ms. Delapaz was prescribed caused weight gain, thyroid problems, adrenal gland problems, and fatigue. Tr. 52:6–11. Petitioner stated that physical therapy helped some but that the IVIG caused "a lot of side effects, and it just became too much." Tr. 52:22–53:3. Petitioner testified that Ms. Delapaz tried a third IVIG treatment and that doctors tried to pre-medicate her to prevent side effects. Tr. 53:9–17. However, Ms. Delapaz's anemia and meningitis returned, and "she had even more intense headaches." Tr. 53:17–21.

Petitioner discussed treatment under Dr. Jarjour, who believed that Ms. Delapaz had dysautonomia. Tr. 54:6–55:7. Petitioner also recalled Ms. Delapaz beginning treatment at the dysautonomia clinic. Tr. 55:8–56:19. Petitioner testified that she followed instructions to stop Ms. Delapaz's medications so she could have an accurate tilt table test. Tr. 57:4–9. Petitioner testified that Ms. Delapaz's tilt table test showed "[s]omething about her nerves not sending the correct signals[o]r not receiving them correctly." Tr. 57:13–14. Petitioner discussed Ms. Delapaz's continuing struggles with urination, and Petitioner testified that Ms. Delapaz's bladder issues continued until she passed away. Tr. 57:15–24. Petitioner stated that the urination difficulties improved somewhat but never fully resolved. Tr. 57:25–58:4.

Addressing whether Ms. Delapaz's treating physicians believed her HPV vaccination caused her symptoms, Petitioner testified that "[t]he immunologists could not agree. They said she would[not] say it on record." Tr. 58:5–10. She continued that "Dr. Jones[] . . . immediately thought that that could be it[,] and she strongly believed that it was that, and she did try to reach out to other patients to see if they had the vaccine. She talked to her colleagues to see if they had seen it." Tr. 58:11–15. Petitioner testified that Ms. Delapaz's treaters were divided on whether she experienced an allergic reaction to the HPV vaccine. Tr. 61:7–11. However, doctors, including Dr. Jones, advised Ms. Delapaz to not receive further doses of the HPV vaccine because it was too risky. Tr. 61:12–62:1.

Petitioner testified that Ms. Delapaz experienced some improvement in her symptoms between 2013 and her passing in 2020. Tr. 59:18–20. Petitioner testified that Ms. Delapaz began urinating more and that she was able to return to school and begin working. Tr. 59:21–60:2. Petitioner testified that Ms. Delapaz began taking "natural medicine and treatment and for three or four months it helped her tremendously. To the point where she was working full time, she started college with [a] full-time internship, [and was] go[ing] out and see[ing] friends." Tr. 60:2–6.

Petitioner stated that Ms. Delapaz was not "strong, strong[,] . . . but she was working her way up to it[]" with physical therapy and exercise. Tr. 60:7–12.

III. Medical Literature

A. Autonomic Ganglia: Target and Novel Therapeutic Tool

Petitioner filed an article by Vernino et al.,[58] co-authored by Respondent's expert, Dr. Low, to help explain AAG. Pet'r's Ex. 33, ECF No. 50-5. Vernino et al. describe the autonomic system as "groups of neurons (ganglia) with extensive synaptic connections outside the central nervous system." *Id.* at 1–2. These peripheral nerves "originate with cholinergic motor neurons in the brainstem and spinal cord that project to the periphery." *Id.* at 2. The autonomic neurons in the periphery synapse with neurons in the autonomic ganglia and each other. *Id.* The transmission "is mediated by acetylcholine acting on nicotinic acetylcholine receptors (AChRs)." *Id.* In AAG, "defective ganglionic transmission will lead to diffuse autonomic failure." *Id.* Also known as acute pandysautonomia and autoimmune, idiopathic, or subacute autonomic neuropathy, "[g]anglionopathy is the preferred term because experimental data indicate that the primary pathophysiology of this disorder affects autonomic ganglia rather than damage to autonomic nerve fibers." *Id.*

Although "[p]atients with [AAG] often have antibodies against the ganglionic AChR[,]" about 50% of patients with subacute AAG do not. *Id.* at 2–3. High antibody levels are a good indicator of the most severe and widespread manifestation of autonomic failure. *Id.* at 3. Typical patients are "previously healthy, young or middle-aged individuals[,]" and there is a "female predominance of about 2 to 1." *Id.* at 2. Within a few days or weeks, AAG patients suffer "diffuse autonomic failure affecting all limbs of the autonomic nervous system[,]" with OH, widespread anhidrosis,[59] dry mouth and eyes, urinary retention, impaired pupillary light response, fixed heart rate, and/or gastrointestinal dysmotility. *Id.* Some patients present with "prominent parasympathetic deficits or cholinergic deficits [] without [OH]." *Id.* at 4. Postural orthostatic tachycardia syndrome ("POTS")[60] "is the most common form of orthostatic intolerance without [OH]." *Id.* Other common accompanying symptoms include "anorexia, early satiety, postprandial abdominal pain, vomiting, diarrhea, constipation, [and] intestinal pseudoobstruction [sic]." *Id.* at 2. Approximately one-quarter "of patients describe minor sensory symptoms, such as tingling, but objective sensory loss is not present." *Id.* at 3.

An antecedent viral syndrome is recorded in many cases, but recent immunization or minor surgical procedures have also been noted. *Id.* at 2. This chronology and the clinical presentation "suggest an immune-medicated basis for this disease." *Id.* at 3. Even in patients that do not harbor AChR antibodies, the pathogenesis is unknown but presumed autoimmune, "based on the clinical similarities to seropositive patients." *Id.* The article supposes that "[t]hese patients might harbor

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[58] Steven Vernino et al., *Autonomic Ganglia: Target and Novel Therapeutic Tool*, 70(20) NEUROLOGY 1926 (2008).

[59] Anhidrosis is "absence or severe deficiency of sweating, usually due to absence or paralysis of the sweat glands or to obstruction of the sweat ducts." *Dorland's* at 90.

[60] POTS is characterized by "a group of symptoms (not including hypotension) that sometimes occur when a person assumes an upright position, including tachycardia, tremulousness, lightheadedness, sweating, and hyperventilation; this is seen more often in women than in men, and the etiology is uncertain." *Dorland's* at 1815.

ganglionic AChR antibodies that do not circulate in the blood because they are entirely sequestered in the tissues[,]" or "some patients may have antibodies against other components of the autonomic ganglionic synapse or against targets elsewhere in the autonomic nervous system." *Id.* Vernino et al. state that "[t]he classic severe subacute form of AAG is associated with high levels of ganglionic AChR antibodies." *Id.* at 3–4. There are three additional clinical AAG phenotypes identified in the article: "1) a chronic or slowly progressive diffuse autonomic failure, similar to pure autonomic failure, 2) limited autoimmune autonomic dysfunction, including isolated gastrointestinal dysmotility, or cholinergic autonomic failure, and 3) postural tachycardia syndrome." *Id.* at 4.

B. Case Studies

Petitioner's expert, Dr. Blitshteyn, relied on two Medscape articles, both by Chustecka, that describe a series of case studies in Denmark and a collection of international case studies, including the Denmark cases. *See* Pet'r's Ex. 43, ECF No. 50-15;[61] Pet'r's Ex. 44, ECF No. 50-16.[62] Citing an article published in the *Danish Medical Journal*, Chustecka noted that the Danish cases included fifty-three patients referred to a Denmark hospital's syncope unit with "symptoms consistent with pronounced autonomic dysfunction[,] including different degrees of orthostatic intolerance, severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort[,] and widespread pain of a neuropathic character." Pet'r's Ex. 43 at 2. The symptoms were "suspected adverse effect[s] of vaccination with the quadrivalent HPV vaccine, Gardasil." *Id.* Half of the patients in the study were ultimately diagnosed with POTS, but the authors cautioned that "POTS should probably be looked upon as a symptom secondary to another yet identified condition rather than as a disease entity of its own[.]" *Id.* They noted that much is unknown about the etiology of POTS and "the prevalence of POTS is most common in the same subset of the population that are receiving the HPV vaccine (young women)," further complicating the discussion. *Id.* Consequently, the authors noted that their "findings do not confirm or dismiss a causal link to the HPV vaccine[.]" *Id.* The manifestation of symptoms ranged from zero to fifty-eight days in the reported cases, and appeared following the receipt of the first, second, and in some instances, third vaccine. *Id.* This article also briefly refers to similar work done by Japanese researchers and in the United States. *Id.* In Japan, researchers "reported on 'peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine[.]'" *Id.* In the United States, Petitioner's expert, Dr. Blitshteyn, "described six patients who developed new-onset POTS from [six] days to [two] months after HPV vaccination." *Id.* Dr. Blitshteyn wrote, "[t]hree patients also had neurocardiogenic syncope, and three patients were diagnosed with possible small fiber neuropathy[.]" *Id.*

The second Medscape article discussed a case study published in *Clinical Rheumatology* that reported on forty-three individuals from thirteen countries, who, after a mean period of four years after HPV vaccination, "continue to have incapacitating symptoms and remain unable to attend school or work[.]" Pet'r's Ex. 44 at 6. Treaters in Mexico City described "[a] disabling

[61] Zosia Chustecka, *Safety Profile of HPV Vaccines Under Review in Europe*, MEDSCAPE (July 13, 2015), http://www.medscape.com/viewarticle/847841.

[62] Zosia Chustecka, *Case Reports of 'Syndrome' Appearing After HPV Vaccination*, MEDSCAPE (Sept.18, 2015), http://www.medscape.com/viewarticle/851186.

syndrome of chronic neuropathic pain, vexing fatigue, and profound autonomic dysfunction [that] may appear after HPV vaccination[.]" *Id.* Chustecka noted that "HPV vaccines have been given to more than [seventy-two] million people worldwide," and that "experts point out that all of these publications are case reports with no control subjects, and cannot determine causality." *Id.* She noted that "[h]ealth officials at the US Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) emphasize that controlled clinical trials in tens of thousands of individuals plus post licensure monitoring of millions of individuals have found no casual association between HPV vaccination and atypical pain syndrome or autonomic dysfunction." *Id.*

IV. Experts

A. Expert Review

1. Petitioner's Expert, Svetlana Blitshteyn, M.D.

Dr. Blitshteyn received her medical degree from the State University of New York School of Medicine and Biomedical Sciences in 2002. Pet'r's Ex. 80 at 2, ECF No. 124-15. She completed a residency in internal medicine at State University of New York at Buffalo in 2003 and a neurology residency at the Mayo School of Graduate Medical Education in 2007. *Id.* at 1–2. She began working as a clinical assistant professor at University of Buffalo Jacobs School of Medicine and Biomedical Sciences in 2008, and she became a clinical associate professor in 2022. *Id.* at 1. Dr. Blitshteyn is board certified in neurology by the American Board of Psychiatry and Neurology. Pet'r's Ex. 28(a) at 1. She "specialize[s] in autonomic disorders, a specialty [she] learned during [her] neurology training at the Mayo Clinic, where the autonomic function testing was invented." *Id.* Dr. Blitshteyn is the director of the Dysautonomia Clinic and Amherst Neurology, which she founded in 2009. *See* Pet'r's Ex. 80 at 1. Through her work at the clinic, Dr. Blitshteyn has "personally evaluated close to a thousand patients with various autonomic disorders . . . ." Pet'r's Ex. 28(a) at 1. Her work also includes monitoring neurosurgeries and providing second opinions through a consulting company. Tr. 11:23–12:3. She has also worked on various types of legal cases since 2010. Tr. 12:3–5. Dr. Blitshteyn has received numerous awards, belongs to professional organizations, and has served as an ad hoc reviewer for medical journals. Pet'r's Ex. 80 at 2–4.

2. Respondent's Expert, Phillip Low, M.D.

Dr. Low obtained his medical degree from the University of Sydney in 1976. Resp't's Ex. Y at 1, ECF No. 121-1. He completed post-doctoral fellowships at the Mayo Clinic's department of neurology in Rochester, Minnesota and Northwestern University's department of pharmacology. *Id.* Dr. Low finished his neurology residency in Rochester, Minnesota in 1980. *Id.* He has been a professor of neurology at the Mayo Clinic College of Medicine and Science since 1984, and he was an assistant and associate professor between 1978 and 1984. *Id.* at 1–2. In addition to having treated patients at the Mayo Clinic in Minnesota since 1978, Dr. Low "founded the Mayo Autonomic Laboratory in 1983 and headed it for [twenty-four] years." *Id.* at 1; Resp't's Ex. A at 1. The laboratory "studies 4000 patients per year with autonomic disorders." Resp't's Ex. A at 1. Dr. Low has "published over 400 publications in peer-reviewed journals [] and [four] books on autonomic disorders." *Id.* He has "described novel autonomic disorders including [AAG, POTS], chronic idiopathic anhidrosis[,] and autoimmune and inherited neuropathies." *Id.* Dr. Low has also "developed and validated autonomic function tests that have become the nation's

standard." *Id.* Dr. Low developed the QSART and thermoregulatory sweat tests, and he "adapted the tilt table test from research into practice by providing [an] adequate number of normative data[.]" Tr. 18:10–23. He has "published extensively on orthostatic intolerance, POTS, the synucleinopathies[,] and the autoimmune autonomic ganglionopathy." Resp't's Ex. A at 1. Dr. Low testified that he spends about half of his time treating patients and half in research. Tr. 19:11–15. He is board certified by the American Board of Psychiatry and Neurology. Resp't's Ex. Y at 1. He is a member of professional societies, works on journals, and has received numerous grants and awards. *Id.* at 2–13.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Blitshteyn

Dr. Blitshteyn authored a brief summary opinion and two expert reports[63] and testified at the entitlement hearing. Pet'r's Exs. A, 28(a), 50; Tr. 10–15, 76–162, 169–210, 287–295. In her first full expert report she began with a summary of Ms. Delapaz's medical history. Pet'r's Ex. 28(a) at 2–3. Dr. Blitshteyn characterized Ms. Delapaz's severe immune-mediated autonomic neuropathy and autoimmune dysautonomia as AAG. *Id.* at 4. She defined ganglionopathy as the abnormal pathophysiology at "a collection of neurons from which autonomic nerve fibers arise . . . ." *Id.*

Dr. Blitshteyn noted that [Ms. Delapaz's] condition was described many ways by her treaters, including as "neurocardiogenic syncope, POTS, chronic fatigue syndrome [("CFS")],[64] dysautonomia, autoimmune dysautonomia, immune-mediated neuropathy, autoimmune neuropathy, and perhaps others." *Id.* She described autoimmune dysautonomia as a general term and stated, "if we want to really be precise as to what part of autonomic nervous system was affected, and, you know, what exactly was happening on a very much academic level, we could say cholinergic autonomic neuropathy, immune-mediated cholinergic neuropathy." Tr. 79:15–19. She explained that "[a]ll these terms apply to the same syndrome, and the syndrome is an abnormal autonomic nervous system as confirmed by two autonomic function tests that [Ms. Delapaz] had. Tr. 79:19–22. She explained that the insurance codes for many of these diseases are not always precise "and there is still no ICD-10 code specifically for certain autonomic disorders." Tr. 80:23–81:1. In Ms. Delapaz's case, one of her treaters "correctly used unspecified disorder of the autonomic nervous system[]" and described the condition as "severe autonomic dysfunction." Tr.

[63] In addition to the autoimmune autonomic ganglionopathy claim currently at issue, Petitioner has also previously asserted Table and off-Table claims of anaphylaxis. Immediately prior to the presentation of evidence at the entitlement hearing, Petitioner confirmed that based on the evidence in the record, she would not continue to pursue either anaphylaxis claim. There was no evidence of vaccine-caused anaphylaxis presented at the hearing. Furthermore, there was no asserted biological mechanism for anaphylaxis as a vaccine-caused injury. Although Petitioner's expert discussed anaphylaxis in her reports, it is no longer an alleged injury. To the extent that anaphylaxis is described in a discussion of AAG, that will be included in my analysis.

[64] CFS is characterized by "persistent debilitating fatigue lasting longer than [six] months, with other known medical conditions having been ruled out by clinical diagnosis, accompanied by at least for of the following: significantly impaired short-term memory or concentration, muscle weakness, pain in multiple joints without swelling or redness, sore throat, tender lymph nodes, headaches, unrefreshing sleep, and malaise that lasts more than [twenty-four] hours following exertion." *Dorland's* at 1795.

81:5–8. Dr. Blitshteyn testified that Ms. Delapaz's type of autonomic dysfunction, immune-mediated cholinergic neuropathy, "is a type of AAG." Tr. 82:6–7. Citing Petitioner's Exhibit 33, she stated that Ms. Delapaz's AAG fell under the second phenotype listed by Vernino et al. Pet'r's Ex. 50 at 2. Vernino et al. describe this phenotype as "limited autoimmune autonomic dysfunction, including isolated gastrointestinal dysmotility, or cholinergic autonomic failure[.]" Pet'r's Ex. 33 at 4. She explained that she referred to Ms. Delapaz's condition as AAG "because this is the proper name for her condition as it is defined in the scientific literature." Pet'r's Ex. 28(a) at 4. Dr. Blitshteyn continued that the "experimental data indicate that the primary pathophysiology of this disorder affects autonomic ganglia rather than damage to autonomic nerve fibers." *Id.*

Dr. Blitshteyn described the "typical patient with AAG [as having] widespread autonomic failure affecting all parts of the autonomic nervous system." *Id.* This includes sympathetic failure, which presents as "[OH] [] and widespread anhidrosis" and parasympathetic failure, which "presents as dry mouth, dry eyes, sexual dysfunction, urinary retention, and impaired pupillary light response." *Id.* Dr. Blitshteyn asserted that Ms. Delapaz experienced most, if not all, of these symptoms. *See id.* Dr. Blitshteyn conceded that Ms. Delapaz "did not display [OH] pattern on her autonomic function tests[.]" *Id.* However, Dr. Blitshteyn opined that Ms. Delapaz's "complaints of the orthostatic lightheadedness, dizziness[,] and syncope suggest that indeed [OH] was the underlying mechanism of her orthostatic symptoms in her daily life." *Id.*

Dr. Blitshteyn identified viral illness, minor surgical procedures, and immunizations as common antecedents to AAG. *Id.* at 5. She acknowledged that AAG is "commonly diagnosed using appropriate clinical features and objective evidence obtained via the autonomic function tests that usually reveals widespread autonomic failure and widespread anhidrosis, both of which were found in [Ms. Delapaz's] case." *Id.* Dr. Blitshteyn noted that Ms. Delapaz's case is atypical in that she is among 25% of patients that experience "sensory symptoms such as numbness and tingling []." *Id.* (citing Pet'r's Ex. 33 at 3). Ms. Delapaz also tested negative for ganglionic AchR antibody, but Dr. Blitshteyn noted that this occurs in 50% of patients with AAG. *Id.* Dr. Blitshteyn wrote that the seronegative "patients are presumed to have an autoimmune disorder based on the clinical similarities to seropositive patients." *Id.* She continued that "a possible explanation for the seronegativity is that either these patients harbor ganglionic AChR antibodies that do not circulate in the blood or they have different antibodies . . . that have not yet been identified []." *Id.* Although seronegative, Ms. Delapaz's case was consistent with seropositive cases because she "became severely disabled by the symptoms of dysautonomia and autonomic neuropathy[] . . . ." *Id.* Dr. Blitshteyn asserted that "[Ms. Delapaz's] diagnosis of AAG and excellent response to [IVIG] confirm a definitive autoimmune etiology in [her] case." *Id.*

Dr. Blitshteyn compared AAG to other autonomic disorders that "have been reported to occur after immunization[,]" such as small fiber neuropathy[65] and POTS. *Id.* Due to the nature of these types of conditions, Dr. Blitshteyn asserted that "[a] precise diagnosis of the autonomic disorder can only be established by a physician with knowledge of the autonomic disorders and who has a high index of clinical suspicion in an appropriate clinical setting." *Id.* She identified Gardasil as one vaccine that "has been specifically observed as a possible trigger of the autonomic disorders[] . . . ." *Id.* She noted that studies from Japan and Denmark have identified patients with

[65] Small fiber neuropathy is "a type of neuropathy in which only the small sensory cutaneous nerves are affected." *Dorland's* at 1252.

sympathetic dysfunction following the HPV vaccine. *Id.* at 5–6 (citing Pet'r's Ex. 38, ECF No. 50-10; Pet'r's Ex. 39, ECF No. 50-11).[66] These patients shared symptoms of "orthostatic dysregulation, fatigue, widespread pain, cognitive dysfunction, and significant functional impairment[] . . . ." *Id.* at 6. Dr. Blitshteyn acknowledged that "most of the reported patients appeared to have milder forms of dysautonomia than [Ms. Delapaz]." *Id.* Dr. Blitshteyn also acknowledged that "the European [Medicines] Agencies [("EMA")] concluded in 2015 that there appears to be no evidence of increased prevalence of POTS and [complex regional pain syndrome ("CRPS")][67] after HPV vaccines, [but] concerns . . . remain due to a lack of randomized double-blinded controlled study . . . ." *Id.* (citing Pet'r's Exs. 43–44). The EMA's conclusion is supported by large scale studies, *see* Resp't's Ex. C at 1, ECF No. 55-3,[68] but Dr. Blitshteyn was critical of them. One study was criticized by researchers from an academic center with a syncope unit in Denmark, "citing irregularities, citing bias of each of the – some of the EMA members, you know, with ties to pharma." Tr. 128:12–14. (citing Pet'r's Ex. 46, ECF No. 50-18).[69]

Dr. Blitshteyn also criticized a paper by Doshi et al.[70] because "to make the data more appealing to FDA, [the researchers] have switched from [a] saline placebo to [an] aluminum adjuvant placebo to make the adverse events more even." Tr. 129:3–6 (citing Pet'r's Ex. 67, ECF No. 124-4). Dr. Blitshteyn explained this was problematic because saline exists in our bodies, "[b]ut aluminum, . . . those are salts that can trigger non-IgE-meditated allergic reactions and adverse events." Tr. 129:21–24. As a result, "if you have that as your placebo arm, and then the patient arm is the same aluminum adjuvant plus HPV particles, then it looks all right." Tr. 129:24–130:1. Other complaints from Merck studies included data loss, "irregularities of the trial process and of the fact that some cards on patients who were reporting adverse events were not filed appropriately." Tr. 129:10–13. Dr. Blitshteyn compared these studies to the one done by Jørgensen.[71] Tr. 130–31 (citing Pet'r's Ex. 70, ECF No. 124-6). The Jorgensen study "pulled all of the adverse events from all of the trials on Gardasil[and] . . . on HPV vaccines in general." Tr. 130:15–17. The researchers found "that serious harms were judged 'definitely associated' with POTS or CRPS by blinded physicians. And they did find increased serious harm for POTS [and CRPS] by HPV vaccines." Tr. 131:2–5. Significantly for Ms. Delapaz's case, "they also [found] general harms for the following symptoms: [m]yalgia,[72] fatigue, and headache." Tr. 131:10–11.

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[66] Tomomi Kinoshita et al., *Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine*, 53 INTERNAL MEDICINE 2185 (2014); Louise S. Brinth et al., *Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papilloma virus*, 33 VACCINE 2602 (2015).

[67] CRPS is "a chronic pain syndrome of uncertain pathogenesis, usually affecting an extremity, and characterized by intense burning pain, changes in skin color and texture, increased skin temperature and sensitivity, sweating, and edema." *Dorland's* at 1795.

[68] European Medicines Agency, *HPV vaccines: EMA confirms evidence does not support that they cause CRPS or POTS* (Jan. 12, 2015).

[69] Peter Gøtzche et al., *Complaint to the European ombudsman over maladministration at the European Medicines Agency (EMA) in relation to the safety of the HPV vaccines* (Oct. 10, 2016).

[70] Peter Doshi et al., *Adjuvant-containing control arms in pivotal quadrivalent human papillomavirus vaccine trials: restoration of previously unpublished methodology*, 25(6) BMJ EVIDENCE-BASED MEDICINE 213 (2020).

[71] Lars Jørgensen et al., *Benefits and harms of the human papillomavirus (HPV) vaccines: systematic review with meta-analyses of trial data from clinical study reports*, 9(43) SYSTEMATIC REVIEWS (2020).

[72] Myalgia is muscle pain. *Dorland's* at 1197.

Dr. Blitshteyn noted that Ms. Delapaz had these three symptoms. Tr. 131:11–12. She confirmed that Ms. Delapaz did not have POTS, but stated, "[s]he had worse than POTS and [a] more severe autonomic disorder than POTS." Tr. 131:21–23. As additional support for her analogy, Dr. Blitshteyn referenced Dr. Low's article where he classified POTS as a clinical phenotype of AAG. Tr. 288:10–18 (citing Pet'r's Ex. 33 at 4, ECF No. 50-5).[73] Ms. Delapaz's case of an autonomic disorder post HPV vaccination is an example of what Dr. Blitshteyn sees in her clinic more often than post other vaccinations. Tr. 132:25–133:4. Dr. Blitshteyn noted that "after HPV vaccine, not after flu, not after tetanus, not after MMR, but after HPV vaccine, suddenly there were these young women who became sick." Tr. 133:3–5. She reiterated that she is "very much pro-vaccine," but she could not ignore what she was seeing in her own practice. Tr. 133:9. She added, "because we [cannot prove] causation does[not] mean we have to dismiss, you know, these rare cases that are clearly triggered by a vaccination." Tr. 137:17–20.

Dr. Blitshteyn stated that the non-IgE mediated allergic reaction and AAG allegedly experienced by Ms. Delapaz "share a common pathophysiologic immune-mediated mechanism that is quite complex[.]" Pet'r's Ex. 28(a) at 6. She explained that B cells[74] are activated via molecular mimicry and then "likely recognize a sequence of the recombinant HPV vaccine component as 'self antigen.'" *Id.* This component

> can harbor a homologous stretch of the amino acids similar to the target receptor or target protein of the autonomic ganglia. The result is the formation of the cross-reacting antibody, either to a subunit of the ganglionic AchR receptor, . . . or another protein located at the autonomic ganglia or neuron.

Id. Dr. Blitshteyn asserted that AAG occurs when "[t]he cross-reacting autoantibody interrupts synaptic transmission at the autonomic ganglia . . . ." *Id.* Suggesting that molecular mimicry has been associated with autonomic disease, she submitted an article she published that suggests that several autoantibodies have been associated with POTS. *See* Pet'r's Ex. 42, ECF No. 50-14.[75] She stated that onset of AAG within four weeks of vaccination is an appropriate time frame. *Id.* at 7. She later clarified that in Ms. Delapaz's case, like in most cases, onset is not acute, and "[y]ou[are] not going to pinpoint a day like with an allergic reaction." Tr. 174:24–25.

In Dr. Blitshteyn's opinion, Ms. Delapaz's symptoms "start[ed] right away when she had that reaction with headache and syncope." Tr. 83:15–16. Although Dr. Blitshteyn acknowledged that "syncope is actually the most common reaction to all vaccines[] and [does] not necessarily represent[] anything ominous," she did not believe that Ms. Delapaz's case was typical. Tr. 83:17–21. This is evidenced by Ms. Delapaz's clinical presentation, one day post vaccination, at her pediatrician's office with high blood pressure and high heart rate. Tr. 83:22–84:5. Dr. Blitshteyn distinguished Ms. Delapaz's condition from other immune-mediated neuropathies that take "maybe two to four weeks for the antibodies to form." Tr. 85:3–4. She described an IgE-mediated

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[73] Steven Vernino et al., *Autonomic Ganglia: Target and Novel Therapeutic Tool*, 70(20) NEUROLOGY 1926 (2008).

[74] B lymphocytes are "primarily responsible for humoral immunity," which is "immunity mediated by antibodies." *Dorland's* at 1070, 906.

[75] Svetlana Blitshteyn and Jill Brook, *Postural tachycardia syndrome (POTS) with anti-NMDA receptor antibodies after human papillomavirus vaccination*, IMMUNOL RES (Aug. 25, 2016).

reaction that can develop into anaphylaxis within twenty minutes and then clarified that Ms. Delapaz did not suffer from anaphylaxis. Tr. 84:24–85:8. Ms. Delapaz, Dr. Blitshteyn opined, suffered from a non-IgE-mediated reaction in response to vaccination. Tr. 85:21–25. Dr. Blitshteyn stated that based on the timeline, Ms. Delapaz's reaction "was more subacute, because within three months, she was quite sick." Tr. 87:20–22. In later testimony, Dr. Blitshteyn opined that what happened to Ms. Delapaz "happened within hours." Tr. 172:23. Specifically, Ms. Delapaz's initial immune response "began within hours the chain of events [that eventually developed into t]his entity we call post-vaccination cholinergic neuropathy." Tr. 173:7–9. Dr. Blitshteyn described Ms. Delapaz's symptoms of headache, dizziness, vertigo, and intermittent redness of the face noted during her June 6, 2012 doctor's visit and her "dizziness, extremity weakness, headache, [and] numbness in extremities" reported during a doctor's visit on August 9, 2012, as evidence of continued autonomic symptoms as early as three weeks post vaccination. Tr. 201:20, 178:16–17. Dr. Blitshteyn did not believe that Ms. Delapaz's history of allergies could account for one or more of these symptoms. Tr. 180:11.

In describing autonomic neuropathies and AAG, Dr. Blitshteyn discussed the Vernino et al. article co-authored by Dr. Low. *See* Pet'r's Ex. 33. Specifically, she explained the importance of the acetylcholine receptor. *See* Tr. 89. This receptor "transmits all of the signals in the autonomic nervous system, often [at the] pre-ganglionic and post-ganglionic level." Tr. 89:5–7. Consequently, if "you block the normal transmission of the autonomic nervous system[, then] you end up with quite significant failure." Tr. 89:10–12. This blockage is often caused by antibodies, but in about half of all patients, including Ms. Delapaz, they are not present. Tr. 89:13–15. This type of AAG, seronegative, is similar to the seropositive phenotype, but "it looks like the severity may be less than in those whose antibodies are found at the high level." Tr. 89:18–20. Dr. Blitshteyn reiterated that "[w]e do[not] know" if Ms. Delapaz had other relevant antibodies that we do not currently test for in the United States, or if she had antibodies at some point that would have shown up if she was tested earlier. Tr. 94:22–95:5. She explained that "if someone presents with post-vaccination neuropathy of any kind, we presume it to be autoimmune because after vaccination you get a huge stimulation of your own immune system, and sometimes, you know, the body wrongfully recognizes the parts from the vaccine to the parts of your own proteins and begins to attack them[] . . . ." Tr. 95:19–23. How that autoimmunity manifests, including as an autonomic neuropathy, "depends probably on where the body attacks, and Dr. Low describes it in all of this papers." Tr. 95:25–96:2. She discussed new developments with POTS and long COVID stating, "this kind of area of immunology is very much evolving." Tr. 96:14–15.

Dr. Blitshteyn was critical of the American studies done on AAG patients by Drs. Vernino and Low. *See* Tr. 89–91. She noted the widely used antibody testing was singular and other countries tested for other types of relevant antibodies. Tr. 89:24–90:12. She also noted that American studies were done on middle-aged individuals above the age of fifty. Tr. 90:25–91:2. The presentation of a teenager, "whatever her presentation is, is not going to be like the studies shown on, you know, [fifty-five]-year-old individuals with AAG." Tr. 91:9–11.

Dr. Blitshteyn noted that the "most common precipitating factor for AAG is viral illness[,]" followed by systemic autoimmune disorders, and cancer in older individuals. Tr. 91:24–92:66. Currently, there are "zero studies, zero, on post-vaccination neuropathies from Gardasil or actually any other vaccine," save new COVID trials. Tr. 92:7–10. Despite that, Dr. Blitshteyn noted that

Dr. Low also identified immunization as a potential trigger for neuropathy. Tr. 92:21–93:2. The rarity of AAG and post-vaccination illness makes it difficult to better study and understand this relationship. Tr. 93:13–23. Dr. Blitshteyn also noted that the disease is not diagnosed well nationally or globally. Tr. 93:21–23. She opined that Ms. Delapaz had "a rare presentation[,] and that[is] why it[is] not going to be fitting into these nice little boxes that we want our patients to go in when we diagnose them." Tr. 94:13–16.

Young girls that present with Ms. Delapaz's autonomic symptoms along with anxiety, pain, and migraines will likely be misdiagnosed, according to Dr. Blitshteyn, without "the right doctors who can even recognize this [type of autonomic dysfunction]." Tr. 97:19–98:4. Consequently, Ms. Delapaz was able to undergo a battery of appropriate tests. Tr. 98:11–15. Dr. Blitshteyn noted that Ms. Delapaz produced no sweat during her QSART test, consistent with cholinergic neuropathy. Tr. 103:23–104:14. Dr. Blitshteyn also noted that Ms. Delapaz was in the fourth percentile for her Valsalva ration, and despite not qualifying for a POTS diagnosis, her supine heart rate was abnormal. Tr. 104:17–105:12. Using the CASS that Dr. Low invented, Ms. Delapaz's treaters "gave her a 6, and she[is] – because, you know, there is a 3 for lack of sweating and 3 for cardiovagal problem." Tr. 105:17–20. Dr. Blitshteyn noted that Ms. Delapaz "did not have a problem with adrenergic response, so her score was zero." Tr. 105:21–22. Her total score "is 6, which is moderate, moderate autonomic failure." Tr. 105:22–23. In response to Dr. Low's criticism, Dr. Blitshteyn noted that Ms. Delapaz's mother confirmed that her daughter had stopped taking her medications for forty-eight hours prior to QSART testing pursuant to her doctor's instruction. Tr. 107:24–108:19, 109:7–10. Dr. Blitshteyn also pointed out that "there are two QSARTs in [Ms. Delapaz's] case, months apart[,]" with her on the same medications and done by the same lab. Tr. 109:25–110:2. There was zero sweat on the first one, but there was sweat output during the second. Tr. 110:2–3. This, in Dr. Blitshteyn opinion, is consistent with Ms. Delapaz's medical record of autonomic disorder that improved. Tr. 110:11–21. She emphasized that autonomic dysfunction occurs on a spectrum, and she is "going by what other neurologists have found[.]" Tr. 111:10–14. She did not contest Dr. Low's assertion that Ms. Delapaz's CASS score should have been a five. She testified that she would "go with Dr. Low's score any day. If he says five, it must be five." Tr. 115:21–22. However, she also stated that five or six "still indicates [a] moderate degree of autonomic failure[.]" Tr. 115:25–116:1. Dr. Blitshteyn did not buy Dr. Low's consideration of parasympathetic overactivity in Ms. Delapaz's case. She testified that "with sympathetic overactivity, interestingly, you expect increased perspiration[] . . . ." Tr. 117:11–12. Ms. Delapaz "did[not] have that clinically, and also she did[not] have that on objective testing. She had hypo, hypo response with[] . . . decreased sweating, and decreased bladder, and her pupils may have been[] . . . sluggish at times . . . ." Tr. 117:15–19.

Dr. Blitshteyn acknowledged Dr. Low's expertise multiple times during her testimony. When asked about Dr. Low's statement that Ms. Delapaz's lack of sweat in four locations during the QSART indicated that medications were suppressing sweat, Dr. Blitshteyn stated, "[she] will defer to Dr. Low. [She is] no expert on QSARTs at all, so [she is] going to defer to the expert who invented this test[.]" Tr. 109:11–18. However, Dr. Blitshteyn noted that, based on reports she had read, "the interpreter [of a QSART] will always put there that the reduced sweat output may have been due to medication side effect." Tr. 109:19–22. During my questioning regarding distinguishing AAN from AAG, Dr. Blitshteyn testified that "Dr. Low will be way better

explaining the pre-ganglionic to post-ganglionic with the sweat test that he invented." Tr. 140:8–10.

Dr. Blitshteyn commended Dr. Jones who "did absolutely the right thing by saying[] . . . , something happened after this vaccination, some kind of autonomic problem, and . . . – probably, . . . [given] the severity of it, and the fact that the autonomic tests show cholinergic immune-mediated neuropathy, . . . she [rightfully] ordered IVIG." Tr. 98:15–23. Dr. Blitshteyn testified that she was not surprised by Ms. Delapaz's reaction to the IVIG. Tr. 100:4–7. The reaction was typical because Ms. Delapaz never got any pretreatment with medications like steroids, fluids, antihistamines, and Tylenol. Tr. 100:11–14. Dr. Blitshteyn explained that any "improvement [post IVIG] is both subjective and objective in these patients." Tr. 101:2–3. She continued that she "do[es not] think the improvement is recovery[] . . . but more like[that the] . . . symptoms are more manageable." Tr. 101:6–8. She added that it was "too bad that they did[not] do IVIG every month, because most of our patients need maintenance. It[is] not a one-time kind of treatment." Tr. 101:12–14. Dr. Blitshteyn stated that "a lot of our dysautonomia patients get it actually on a weekly basis, or biweekly." Tr. 101:20–21. She was not surprised that Ms. Delapaz had deteriorated three months after receiving treatment. Tr. 101:22–23. However, Dr. Blitshteyn noted that Ms. Delapaz went from a CASS score of "six in December [of 2012] to one in February of 2013."[76] Tr. 106:11–12. This is a "significant improvement[.]" Tr. 106:13. Notwithstanding the reaction to IVIG, Dr. Jarjour described her autonomic condition as "some kind of resolving immune-mediated process[]" during a March 6, 2013[77] follow-up visit, and Dr. Blitshteyn agreed with this description Tr. 106:16–17. Dr. Blitshteyn attributed the change in Ms. Delapaz's condition to her IVIG treatment, stating that "the only thing that was different is IVIG, which is what it[is] designed to do[. It is] designed to[] . . . help with circulating antibodies and inflammatory process." Tr. 106:20–23. She concluded that the "clinical response of [Ms. Delapaz] is very much in keeping with exactly what is written and what we[are] saying is that it was an immune-mediated cholinergic neuropathy that was much improved with [an] IVIG round." Tr. 107:19–23.

Comparing AAG to Guillain-Barré Syndrome ("GBS"),[78] Dr. Blitshteyn opined that a vaccine can cause AAG, "because vaccines can lead to [GBS], and that[is] a peripheral neuropathy." Tr. 120:4–6. It follows, Dr. Blitshteyn reasoned, that vaccines "can lead to any kind of neuropathy, including AAG, including cholinergic neuropathy, including small fiber neuropathy." Tr. 120:6–8. She conceded that there are no supporting studies for this proposition and pointed to Dr. Low's study that was cancelled due to insufficient numbers. Tr. 120:15–121:1. She opined that "these patients exist, they are happening, but they[are] misdiagnosed, or brushed off, because we[are] all afraid that this will be used as a weapon against vaccination." Tr. 122:5–8. Despite "the party line . . . that, no, vaccines do not cause POTS or AAG or small fiber neuropathy, because causation is very hard to prove[,]" there are individual cases from which that

[76] It is unclear whether Ms. Delapaz's February 2013 CASS score of 1 is noted specifically in the medical records. However, Dr. Blitshteyn's assertion is consistent with Dr. Jarjour's discussion of Ms. Delapaz's February 21, 2013 autonomic function testing. *See* Pet'r's Ex. 25 at 874.

[77] Dr. Jarjour referenced Ms. Delapaz's autonomic testing on February 21, 2013, and noted, "resolving systemic illness that appears to be autoimmune in nature without proof however of any autoantibodies." Pet'r's Ex. 25 at 877.

[78] GBS is "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection." *Dorland's* at 1802.

conclusion can be drawn. Tr. 122:19–123:4. Dr. Blitshteyn conceded that "case series are the lowest level of evidence, always has and always will be, but . . . there are arguments from researchers and philosophers and policy makers that anecdotal evidence in the form of case reports is still evidence, especially when it comes to poorly diagnosed, poorly researched, and rare disorders[.]" Tr. 148:4–12. She opined that case reports "should not be dismissed as[] . . . a whole lot of nothing because they are there to alert [the] scientific community[t]hat something [] might be going on" Tr. 148:4–15. The scientific community was alerted with her six case reports, the fifty reported in the Danish study, the Japanese study, etc. Tr. 148:16–23. Later in her testimony, Dr. Blitshteyn testified that "in some exceptional situations like post-Gardasil autonomic disorders, [and] immune AAG as a disorder in general[,] we have to make exception[] and look at case series and case reports as a stronger evidence than it actually is for things like heart disease or diabetes." Tr. 204:16–20.

Dr. Blitshteyn was asked how Gardasil can cause AAG. She explained that "the way [she] put this [process] together is that to say there was an IgE-mediated reaction. Tr. 123:14–16. She continued that "it all has to do with that this aluminum salt [found in the vaccine] is a very important trigger of T helper 2[79] immune response[] . . . ." Tr. 123:18–20. She explained that "this aluminum also can trigger basal cells[80] and mass [sic] cells to secrete histamine[81] and all other mediators, which is a non-IgE-mediated allergic reaction[] . . . ." Tr. 123:20–23. Dr. Blitshteyn submitted a Medscape article[82] to support that "non-mediated-IgE mast cell and basophil degranulation"[83] can result from substance triggers, such as opiates. Pet'r's Ex. 31 at 2, ECF No. 50-3. After acknowledging that she is not an immunologist, Dr. Blitshteyn continued that "this aluminum adjuvant triggers . . . a cascade of events, and what[is] called NLRP3 system[] . . . ." Tr. 124:9–11 (citing Pet'r's Ex. 47, ECF No. 50-19).[84] This immune system response produces the pro-inflammatory cytokines,[85] "IL-4, IL-18, probably interferons as well there, [and] . . . then these cytokines activate T helper 2 cells, and then the T helper 2 cells activate B cells, because remember, the antibodies are produced from B cells." Tr. 124:17–21. Molecular mimicry occurs when the activated B cells "recognize[] a portion of vaccines and the portion of your own protein to the B acetylcholine receptor, could it be alpha or beta, or maybe it[is] another component, they recognize that they attack it with antibodies." Tr. 124:23–125:5. In Ms. Delapaz's case, Dr. Blitshteyn

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[79] T lymphocytes are "the cells primarily responsible for cell-mediated immunity[.]" *Dorland's* at 1071.
[80] Basal cells are "a type of keratinocyte found in the basal layer of the epidermis." *Dorland's* at 310.
[81] Histamine is "found in all body tissues, particularly in the mast cells and their related blood basophils, the highest concentration being in the lungs." *Dorland's* at 851. Mast cells are "a type of migrant connective tissue cell with basophilic, metachromatic, cytoplasmic granules that contain histamine and heparin in humans . . . ." *Id.* at 315. Basophils are "structure[s], cell[s], or other histologic element[s] that . . . contain vasoactive amines such as histamine and serotonin, which are released on appropriate stimulation." *Id.* at 201.
[82] Becky Buelow, *Immediate Hypersensitivity Reactions*, MEDSCAPE, Feb. 9, 2015, http://emedicine.medscape.com/article/136217.
[83] Degranulation is the "release of the contents of secretory granules from the cell by fusion with the plasma membrane." *Dorland's* at 475.
[84] Stephanie C. Eisenbarth et al., *Crucial role for the Nalp3 inflammasome in the immunostimulatory properties of aluminum adjuvants*, 453 NATURE 1122 (2008).
[85] Cytokine is "a generic term for nonantibody proteins released by one cell population (e.g., primed T lymphocytes) on contact with a specific antigen, which act as intercellular mediators, as in the generation of an immune response." *Dorland's* at 460.

testified, there was such a reaction by a currently unidentified antibody. Tr. 125:10–17. Dr. Blitshteyn believes "it could have been to a different subunit of the same receptor" as [Alpha 3], but she did not go further than that during her testimony. Tr. 125:15–17. She again referenced GBS, stating that "it[is] a very similar kind of scenario, but a different component of the autonomic nervous system is attacked." Tr. 127:5–11. In addition, Dr. Blitshteyn cited articles that she claimed showed "evidence for autoimmunity with cross-reacting antibodies in cases of neurologic syndromes after HPV vaccine . . . ." Pet'r's Ex. 50 at 5. She cited a study by Takashi et al.,[86] which she stated showed "patients with neurologic symptoms [and with] abnormalities in the spinal fluid consistent with neuro-inflammation and neuro-immune process" post Gardasil vaccination. *Id.* (citing Pet'r's Ex. 56, ECF No. 62-3). She noted that the researchers found "increased pro-inflammatory cytokines and antibodies to" certain receptors. *Id.* (citing Pet'r's Ex. 56). She also cited, but did not file, a study by Brinth et al., in which Dr. Blitshteyn claimed "adrenergic antibodies were found in 96% of 51 HPV-vaccinated patients with dysautonomia symptoms vs. 7% in the control group []." *Id.*

During my questioning, I asked Dr. Blitshteyn to explain how her theory is distinguishable from the theory of aluminum adjuvant induced autoimmunity ("ASIA"). Tr. 189:19–20. Dr. Blitshteyn explained that she was not very familiar with ASIA and that she had "not reviewed one paper with ASIA for this case[.]" Tr. 189:22–190:2. However, Dr. Blitshteyn filed an article that lists ASIA as a keyword and mentions ASIA twenty-four times. Pet'r's Ex. 41, ECF No. 50-13.[87] Dr. Blitshteyn admitted that she had "no clue" whether Ms. Delapaz would have ultimately developed a neuropathy if she had been vaccinated with a different adjuvanted vaccine. Tr. 191:12–15. She opined that "if it was aluminum [adjuvant], then we would have so many AAGs walking around[] . . . ." Tr. 194:6–8. In this case, "[t]he starting point is aluminum," but "[t]he ending point is [Ms. Delapaz's] body cross-reacting with vaccine components." Tr. 194:12–15. She clarified her statement that "it was[not] the vaccine protein sequences that caused an allergic reaction." Tr. 194:17–18. To identify the specific peptides that cross-reacted, "we would have to look at this acetylcholine receptor subunit sequence and then go back and see if the IL-1 protein of the HPV, which is that sequence, if it has homologous sequences." Tr. 195:2–10. Dr. Blitshteyn referenced Dr. Low's mice model wherein "the animal was immunized with acetylcholine receptor and then developed this kind of AAG, animal model, and then when they removed it with plasmapheresis, the animal went back to normal." Tr. 198:12–16. Although unable to identify the specific peptide chains, Dr. Blitshteyn stated that "[t]here should be some kind of antibody that is creating this neuropathy." Tr. 199:16–17.

I asked Dr. Blitshteyn for further clarification of how an allergic reaction triggers an autoimmune reaction. Tr. 186:3–5. She called it "the million dollar question." Tr. 186:6. She added that "it will be a guessing game for [her] when there is an end to an allergic process." Tr. 191:2–3. Dr. Blitshteyn acknowledged that any "allergic process, whether it[is] IgE or not, does have an end, and cannot be continued to be[] . . . perpetuated." Tr. 191:4–6.

[86] Yukitoshi Takahashi et al., *Immunological Studies of cerebrospinal fluid from patients with CNS symptoms after human papillomavirus vaccination*, 298 J. NEUROIMMUNOLOGY 71 (2016).
[87] Benjamino Palmieri, *Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature*, IMMUNOL RES (Aug. 9, 2016).

On cross-examination, Dr. Blitshteyn was asked specifically if autoimmune autonomic neuropathy ("AAN") and AAG are the same condition. Tr. 139:17–19. She explained that although related, "AAG would be more extensive and more profound because this G part is on all of the autonomic, both sympathetic and parasympathetic, the ganglia is very important." Tr. 140:1–4. Ganglionopathy results in "widespread autonomic failure, while "the N part refers to just the nerve part, not actually the body." Tr. 140:5–8. Dr. Blitshteyn testified that in Ms. Delapaz's "chart, the AAN, AAG[,] and autonomic dysautonomia are all used interchangeably for that one problem that she[is] having." Tr. 140:17–19. She identified Dr. Low as the expert in AAG, but she then explained that AAG is a "failure of the autonomic transmissions of all types. With the AAN, we[are] saying it[is] a neuropathy, more in the small fiber kind of category." Tr. 141:3–5. Dr. Blitshteyn clarified that she believes Ms. Delapaz "suffered from cholinergic immune-mediated neuropathy[,]" but she is using "AAG" because she is "someone in neurology who uses the term in the community setting." Tr. 141:17–23.

Dr. Blitshteyn was asked if AAG specifically has ever been connected to molecular mimicry in the medical literature, including her own. Tr. 151:19–21. She explained that "it[is] a legal hypothesis[,]" but there have not been any studies on mice or humans. Tr. 151:22–152:1. She then noted that Dr. Low's own writings acknowledged "cases after immunization." Tr. 152:15–16. She testified that he described immunization and cancer, for another example, as triggers for autoimmune disease." Tr. 153:2–6 (citing Pet'r's Ex. 33). On recall, Dr. Blitshteyn noted exactly where Dr. Low defined the relationship between POTS and AAG that serves as the basis for her analogy. Tr. 288:2–20. She testified:

> So this reads several additional clinical phenotypes of AAG may be defined. One, a chronic or slowly progressive diffuse autonomic failure, similar to pure autonomic failure; two, limited or continued autonomic dysfunction, including isolated gastrointestinal issues, or cholinergic autonomic failure. Remember how I said [Ms. Delapaz's] was number two under his classification system? And three, postural tachycardia syndrome. So this is where I'm obtaining my information from this article.

Tr. 288:10–20 (citing Pet'r's Ex. 33 at 4).

2. Respondent's Expert, Dr. Low

Dr. Low, a pioneering expert on autonomic function and disease, authored two expert reports and testified at the entitlement hearing. Resp't's Exs. A, O; Tr. 16–24, 211–285, 295–301. During his testimony, he gave a broad overview of dysautonomia, which he characterized as a terrible, vague term. Tr. 213:18. Dysautonomia "simply means that there is something awry with the autonomic nervous system." Tr. 213:19–20. The autonomic nervous system "controls all of the important functions like blood pressure, heart rate, sweating, bowel, bladder, sexual function, et cetera." Tr. 212:2–7. Dr. Low explained that "normal people" can experience dysautonomia during a panic attack, for example. Tr. 213: 21–23. Autonomic neuropathy is a more specific form of dysautonomia wherein there "is the structural lesion of the peripheral nerve." Tr. 213:5–6. He wrote that AAG is a type of autonomic neuropathy that was so named because his team "found an antibody that can cause AAG[,]" and "the site of the lesion was at the autonomic ganglion[] . . . ." Resp't's Ex. A at 2. Dr. Low specified that AAG is "caused by an Alpha 3 acetylcholine receptor

antibody, also known as ganglionic antibody." Tr. 216:2–6. He commented on Dr. Blitshteyn's testimony that other antibodies may be involved, and he noted that Dr. Vernino, his colleague, examined the entire range from Alpha 1 to Alpha 7 antibodies. Tr. 217:10–14. Ultimately, Dr. Low's colleague found that "Alpha 3 was the one that caused this AAG." Tr. 217:12–14. Dr. Low further noted that Beta 4 antibodies, previously discussed by Dr. Blitshteyn, are not associated with AAG. Tr. 217:2–6.

Symptoms typically associated with autonomic neuropathy reflect loss of sympathetic and parasympathetic function. *See* Tr. 213:8–11. For background, Dr. Low explained that "[t]he parasympathetic is the dominant part of the autonomic nervous system. It[is] the one that functions most of the time. The sympathetic is a system of fight or flight." Tr. 212:21–24. Loss of sympathetic function can cause "many things [to go] wrong, like your blood pressure, you have [OH], so that your blood pressure drops when you stand up." Tr. 213:14–16. Damage to the parasympathetic system can result in constipation and the inability to pass urine as well as Adie's pupil,[88] which occurs when "your pupil dilates, and it cannot constrict[.]" Tr. 215:1–22.

Despite Dr. Blitshteyn's reliance on Dr. Low's research in her discussion of POTS and its similarities to AAG, Dr. Low stressed that "POTS and AAG are diametrically opposite disorders." Tr. 224:1–2. For example, "POTS is associated with orthostatic tachycardia[, while o]n the other hand, [in] AAG, heart rate goes down." Tr. 224:2–4. He also noted that "POTS requires that a patient does not have [OH], whereas AAG has [OH] in [seventy] percent of patients." Tr. 224:6–8. CFS is another condition that Dr. Blitshteyn compared to AAG, but Dr. Low pointed out that CFS "is not even an autonomic disorder." Tr. 224:9–10. He testified that "[t]here is no evidence that [these diseases] are caused by immune damage." Tr. 224:13–18. On recall, Dr. Low acknowledged "a form of – a limited form of AAG that looks like POTS." Tr. 299:23–24. He then immediately re-asserted that POTS was not relevant to this case because, "if you take the whole family of POTS, there is no compelling evidence that that is due to an immunologic disorder. I know I sound a bit contradictory when I say that." Tr. 300:18–24.

Dr. Low described AAG in his written report as a "disease so rare that there were only single case reports until [he] supervised a review of Mayo Clinic experience []." Resp't's Ex. A at 2. He defined AAG as "a rare autoimmune disease affecting the peripheral autonomic nervous system causing typically [OH], Adies pupils, [sic] anhidrosis, neurogenic bladder,[89] and gastrointestinal autonomic failure." *Id.* Dr. Low testified that "[t]here are three legs of the diagnostic stool[:]" the presence of a ganglionic antibody, neurogenic OH, and cholinergic autonomic neuropathy. Tr. 217:21–25. The presence of the Alpha 3 antibody can be determined through testing. *See* Tr. 217. Seventy percent of AAG patients express experience OH, wherein "every time [they] stand up, [their] blood pressure drops." Tr. 218:8–10. Dr. Low noted that even without OH, "almost all patients [who undergo an autonomic reflex screen] with AAG have some evidence of adrenergic impairment." Tr. 218:11–15. He distinguished an actual drop in blood pressure from the more common orthostatic intolerance, which is characterized by lightheadedness

[88] Adie pupil, or tonic pupil, is "a usually unilateral condition of the eye in which the affected pupil is larger than the other and has light-near dissociation, responding slowly to accommodation and convergence and reacting to light only after prolonged exposure to dark or light." *Dorland's* at 1532.
[89] Neurogenic bladder is "any condition of dysfunction of the urinary bladder caused by a lesion of the central or peripheral nervous system." *Dorland's* at 219.

when getting up. Tr. 218:25–219:4. The last leg is more the clinical presentation. Dr. Low identified fixed and dilated pupils, loss of sweat, and gastroparesis[90] as symptoms of cholinergic autonomic neuropathy. Tr. 219–221. These symptoms are specific and not to be confused with their non-autonomic iterations: blurry vision, medication-induced anhidrosis, and vomiting due to stomach irritation. Tr. 220–222.

To measure autonomic function, the "nation's standard is the autonomic reflex screen, which evaluates postganglionic sudomotor, adrenergic, and cardiovagal function []." Resp't's Ex. A at 2. The parts of the screen that evaluate adrenergic function, which controls blood pressure, are the Valsalva maneuver and the tilt table test. Tr. 226:10–17. The evaluation looks "at heart rate response to deep breathing and to the Valsalva maneuver" to measure cardiovagal function. Tr. 226:21–25. Dr. Low testified that he "would couple that [screen] with a thermoregulatory sweat test [("TST")] because anhidrosis is so commonly involved." Tr. 226:6–7. Dr. Low indicated that a TST is preferred to a QSART for suspected AAG. Tr. 238:16–25. The TST measures sweat production on "the entire anterior body surface," and the QSART has four test sites that "measure[] only one centimeter" each. Tr. 239:12, 239:17–18. Dr. Low "invented the QSART," because of a potential reaction to the sweat-activating powder used in the original TST. Tr. 241:12–17. He also introduced a new powder that was less likely to produce an allergic reaction. Tr. 241:14–15.

Dr. Low explained that he developed the CASS to measure the degree of autonomic failure experienced in one patient from 0 to 10, based off the screening and testing. Resp't's Ex. A at 2. The scale was compiled from assigned numbers denoting sudomotor failure from 0 to 3, cardiovagal from 0 to 3, and adrenergic from 0 to 4. *Id.* "A total score of 1–3 comprises mild autonomic failure, 3–6 moderate failure, and 7–10 severe autonomic failure." *Id.*

Dr. Low wrote that Ms. Delapaz claimed to have "developed [AAG] as evidenced by changes in sweating and intermittent dilation of her pupils and blurring of vision, reduced frequency of micturition[,] and bowel opening . . . ." *Id.* at 3. He noted that testing in December 2012 "showed absent sweat production at all testing sites by QSART and abnormal deep breathing and Valsalva tests, compatible with severe cholinergic and cardiovagal dysfunction, such that is seen in autonomic neuropathy." *Id.* He also noted Ms. Delapaz's CASS score was 6. *Id.* Dr. Low opined that Ms. Delapaz's CASS score "should [have been] 5, since the Valsalva ratio was almost normal." *Id.* at 4. Despite Ms. Delapaz's test results, Dr. Low concluded that she "did not demonstrate AAG." *Id.* Specifically, Ms. Delapaz "did not have Adies pupils[,] [sic]" she "never had loss of bladder or bowel control[,]" and "OH was never found during her [two] series of autonomic function tests." *Id.* He explained that "[t]he evaluation of adrenergic function was completely normal[,] and the patient did not have OH." *Id.* Furthermore, her QSART showed absent response for all four sites, which, according to Dr. Low, raises a suspicion that three of Ms. Delapaz's medications (hydrocodone, diphenhydramine, and loratadine) completely suppressed her sweat response. *Id.* Dr. Low "would have said something like[,] '[t]here is widespread postganglionic sudomotor autonomic failure or sweat suppression due to medication effect . . . .'" *Id.* He opined that "the [three] points for sudomotor failure is invalid." *Id.* Dr. Low also noted that "[c]ardiovagal function is affected by the same medications[]" and the patient's "level of sympathetic activity." *Id.* Ms. Delapaz's suppressed parasympathetic activity could, in part, "be

[90] Gastroparesis is "paralysis of the stomach, usually from damage to its nerve supply, so that food empties out much more slowly, if at all." *Dorland's* at 757.

due to sympathetic overactivity." *Id.* Dr. Low emphasized that in Ms. Delapaz's case, "there is NO evidence of autonomic failure clinically." *Id.* (emphasis in original).

Dr. Low repeated this sentiment during his testimony. Dr. Low noted Ms. Delapaz's "two tilt table tests[that] both showed that she did not have [OH]." Tr. 229:3–4. Ms. Delapaz "had completely normal adrenergic function." Tr. 229:7–8. He further noted that Ms. Delapaz had "symptoms of orthostatic intolerance, which occurs in people who do[not] have OH." Tr. 229:23–25. He testified that dizziness, headache, and lightheadedness, symptoms that Ms. Delapaz experienced, "are relatively uncommon in AAG, and they tend to be more common is patients who have milder forms of dysautonomia, as occurs in anxiety, stress, et cetera." Tr. 230:1–7. He also explained why he believed that Ms. Delapaz's QSART tests were compromised due to her medication protocol. Dr. Low identified albuterol sulfate, levalbuterol tartrate, naproxen, ondansetron, and lactulose as medications that can cause fainting, headaches, dizziness, lightheadedness, high blood pressure, constipation, and blurred vision. *See* Tr. 233–235. Dr. Low discussed the results of Ms. Delapaz's CASS. He opined that the sudomotor score of three is accurate, but medications she was on interfered with obtaining an accurate result. Tr. 244:12–21. He found the cardiovagal score to be "probably slightly overscored. It probably should be a two, but it[is] generally reasonably close." Tr. 244:24–25. Dr. Low noted that Ms. Delapaz had a score of zero on the adrenergic scale. *See* Tr. 245:22–24. Dr. Low acknowledged that only seventy percent of AAG patients have OH, but "virtually everyone would have some impairment of adrenergic function on autonomic function test." Tr. 245:24–246:1. He testified that her score made him suspicious of an AAG diagnosis. Tr. 245:2.

Dr. Low testified that most importantly, in December of 2012, Ms. Delapaz's medical record indicates that her current medications included hydrocodone, diphenhydramine, and loratadine, and lorazepam. Tr. 236:21–237:12. All of these medications "greatly affect sweating." Tr. 237:2. Dr. Low stated that Ms. Delapaz's treaters should have included in the record documentation of the date she stopped each medication prior to testing. Tr. 242:3–8. Dr. Low opined that even if Ms. Delapaz stopped taking these medications as instructed for forty-eight hours prior to the QSART, "the response would still be impaired." Tr. 240:9–10. He asserted that the TST is a more robust measure of Ms. Delapaz's sweat production that would have been more accurate in the face of her medication regimen. Tr. 238:23–25.

Dr. Low noted that Ms. Delapaz was never found to have neurogenic bladder or gastrointestinal autonomic failure. Tr. 246:25–247:5. Regarding Petitioner's testimony that Ms. Delapaz was going to the bathroom less often despite receiving fluids in the hospital, Dr. Low explained that this did not indicate a neurogenic bladder. Tr. 231–232. He explained that "[i]n fact, if you look at her constellation of symptoms, it[is] almost certainly due to medications. The clue [he] always use[s] is that when you have a neurogenic bladder, they[are] uncomfortable. When it[is] due to medications, patients do[not] complain." Tr. 232:4–8. When asked to compare the 2012 autonomic test results that showed moderate autonomic failure with the 2013 results that were normal, Dr. Low first noted that he did not have the actual 2013 tests to examine. Tr. 247:14–20. However, he noted that Ms. Delapaz had a score of one on the 2013 test "[b]ecause that[is] what the report said." Tr. 247:21–23. He stated, "based on our discussion, then medication effect would likely have been the reason [for the improvement]." Tr. 248:3–4. He noted that there was a "two

months' interval between tests, so that if the patient were not taking medication for some time, the tests could all revert back to normal." Tr. 248:4–7.

An AAG diagnosis, according to Dr. Low, "is a clinical diagnosis, not – you do the autonomic test to confirm clinical findings, you do[not] make it from the basis of just autonomic function tests." Tr. 248:25–249:2. He added, "[t]here is some fallacy in tests." Tr. 249:5. He stated that Ms. Delapaz's case did not clinically meet the criteria for AAG because her "ganglionic antibody [was] negative, [she exhibited] no OH, [she had] normal adrenergic function, and no clinical evidence of cholinergic failure." Tr. 249:6–14. Dr. Low opined that "[s]he may well have had cardiogenic syncope[.]" Tr. 250:7. The autonomic neuropathy diagnosis "came after the autonomic testing done by Dr. Harati. Once he labeled her as cholinergic autonomic neuropathy, that[is] what they all started calling it." Tr. 250:21–25. He stated that autoimmune autonomic neuropathy is not the same as AAG. Tr. 250:13–15. Dr. Low noted that Ms. Delapaz had received diagnoses of stress and anxiety from "multiple other physicians." Tr. 272:25–273:1. With respect to the severity of her symptoms, he opined, "incapacity and the great effect it has on quality of life, while it[is] terrible, are not symptoms of AAG." Tr. 279:9–11.

Dr. Low stated that he "would not have treated [Ms. Delapaz] with IVIG, since she did not have AAG or significant autonomic failure." Resp't's Ex. A at 5. He pointed out that "much of her subsequent course was aggravated by complications of IVIG, with hemolytic anemia and aseptic meningitis with intracranial hypertension." *Id.* He stated that generally, AAG cannot be cured. Tr. 223:6. Dr. Low noted that "IVIG is not FDA approved for treatment of AAG." Resp't's Ex. A at 4; Tr. 223:8–9. He stated that "[t]reatment like IVIG does not generally help." Tr. 223:8–9. His own clinical study on the treatment's efficacy had to be abandoned, "since the disease was too rare that [they] were unable to recruit the necessary number of subjects." Resp't's Ex. A at 5.

Dr. Low discussed the pathogenesis of AAG. He explained that "[y]ou do[not] get an autoimmune autonomic neuropathy due to the acute mediators." Tr. 251:21–22. He described it as a "delayed response," with an appropriate onset of one to six weeks. Tr. 252:2–5. Dr. Low testified that he "searched the records for any mention of symptoms of AAG and the first indication he got was in November[]" when Petitioner noted Ms. Delapaz often had dilated pupils. Tr. 252:14–17. Ms. Delapaz did not have Adie's pupils, and Dr. Low opined that her pupil dilation "was likely due to sympathetic overactivity." Tr. 252:19–20. He continued with a discussion of Ms. Delapaz's medical history, pre and post vaccination. Tr. 252–57. Dr. Low mentioned an acute allergic reaction on August 30, 2012, several months post vaccination. Tr. 253–54 (citing Pet'r's Ex. 25 at 156). The reaction had numerous potential triggers, including dust mites. Tr. 254:18–22 (citing Pet'r's Ex. 25 at 156). Her medical history from that incident notes a history of severe allergic reactions. Tr. 254:12–14 (citing Pet'r's Ex. 25 at 156). Dr. Low identified another medical record from as early as May 4, 2011, wherein Ms. Delapaz suffered from dizziness, headaches, and fatigue. Tr. 255:21–256:4 (citing Pet'r's Ex. 21 at 495). That medical record also notes that Ms. Delapaz was suffering from constipation. Tr. 256:6–14 (citing Pet'r's Ex. 21 at 496). Dr. Low asserted that Ms. Delapaz suffered from many of the initial symptoms Dr. Blitshteyn attributed to her autonomic neuropathy, prior to her vaccination. Tr. 256:19–24. He dismissed Ms. Delapaz's treater's opinion of a four-month history of autonomic symptoms as "autonomic instability[t]hat does not indicate autonomic damage." Tr. 257:10–20. He opined, "[i]f it is vaccine-induced, [he] would expect onset of an entity within six weeks[,] and we found nothing within six months." Tr.

283:7–9. Dr. Low agreed that Ms. Delapaz "developed an allergic reaction with a vaccine, an acute allergic reaction, and that[is] the issue that has been handled by her immunologist." Tr. 284:20–22. Regarding any hypothesis that neurologic symptoms then developed, "there is no linkage between the two." Tr. 284:23–285:1.

Dr. Low agreed with Dr. Blitshteyn that molecular mimicry is a viable mechanism for the development of AAG. *See* Tr. 258–59. Dr. Low testified that they "identified the target, and we have specified what the antigen is, it[is] Alpha 3 acetylcholine receptor." Tr. 259:12–13. This is, in his opinion, "the fatal flaw" in Dr. Blitshteyn's theory. Tr. 258:24. Dr. Low asserted that the "acetylcholine receptor subtype is not in [the] HPV vaccine." Tr. 259:1–2. This further supports his assertion that "AAG has never been described following [receipt of the] HPV vaccine." Tr. 260:7–8. Dr. Low acknowledged the case report that Dr. Blitshteyn filed by Schofield and Hendrickson discussing an eleven-year-old girl who developed POTS and neurocardiogenic syncope post HPV vaccination.[91] He opined that "the case was extremely weak[,]" but at least it involved an autoimmune autonomic neuropathy. Tr. 260:12–15 (citing Pet'r's Ex. 78, ECF No. 124-13). He noted that "the paper was not published in either an autonomic[,] neurologic[,] or immunologic journal." Tr. 260:17–18. He then referenced the consensus statements by the EMA and the American Autonomic Society that did not find association between POTS/CRPS and the HPV vaccine. *See* Tr. 262. Discussing his own paper, Dr. Low clarified during his testimony that "[t]he reference to AAG and immunization is an unreferenced loose association . . . we ask the patient in the previous month preceding your illness, have you had anything unusual . . . . It[is] a non-causative association." Tr. 263:8–15 (citing Pet'r's Ex. 33).

V. Applicable Legal Standards

To receive compensation under the Vaccine Act, Petitioner must demonstrate either that: (1) his condition is a "Table Injury," and therefore resulted from the receipt of a covered vaccine or vaccines within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as amended by 42 C.F.R. § 100.3; or (2) Petitioner's condition is an "off-Table Injury," one not listed on the Table, that resulted from his receipt of a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Ms. Delapaz's claimed injury does not fall within the Vaccine Table. Thus, she must prove that her vaccine was the cause-in-fact of her condition.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that his vaccine was the cause of his injury. § 13(a)(1)(A). A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is enough for recovery. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). The Vaccine Act also requires petitioners to show by preponderant evidence that: 1) "the residual effects or complications of such illness, disability, injury, or condition [lasted] for more than 6 months after the administration of the vaccine," 2) the administration of the vaccine resulted in death, or 3) that

[91] Jill R. Schofield and Jeanne E. Hendrickson, *Autoimmunity, Autonomic Neuropathy, and the HPV Vaccination: A Vulnerable Subpopulation*, 00 CLINICAL PEDIATRICS 1 (2017).

"illness, disability, injury, or condition from the vaccine [] resulted in inpatient hospitalization and surgical intervention." § 11(c)(1)(D).

In cases where the diagnosis is contested, "special masters may find whether a preponderance of evidence supports any proposed diagnosis before evaluating whether a vaccine caused that illness." *Hibbard v. Sec'y of Health & Hum. Servs*, No. 07–446V, 2011 WL 1766033, at *6 (Fed. Cl. Spec. Mstr. April 12, 2011) (citing *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1345–46 (Fed. Cir. 2010)).

In *Althen v. Sec'y of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278 (Fed. Cir. 2005). The *Althen* test requires a petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.* (internal citations omitted).

Specifically, under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question "can [the] vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *aff'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006), *cert. denied*, 551 U.S. 1102 (2007). This may be accomplished in a number of ways. "Reliability and plausibility of . . . pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *Id.* Additionally, "epidemiological studies and an expert's experience, while not dispositive, lend significant credence to the claim of plausibility." *Id.* Medical literature published in respected medical journals is also persuasive. *Id.* "However, publication 'does *not* necessarily correlate with reliability', because 'in some instances well-grounded but innovative theories will not have been published.'" *Id.* (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 593–94 (1993) (emphasis in original)).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1278. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury. *Pafford*, 2004 WL 1717359, at *4. The petitioner "must explain *how* and *why* the injury occurred." *Id.* (emphasis in original) (internal citations omitted).

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an

extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health and Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not "binding on the special master or court." § 13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.*

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen,* a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("[T]he inoculation is not the cause of every event that occurs within the ten[-]day period. . . . Without more, this proximate temporal relationship will not support a finding of causation.") (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs.*, 98 Fed. Cl. 719, 726 (2011). Consequently, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008); *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that Respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" § 13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (explaining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

Although special masters have the discretion to be informed by past rulings and experiences, case-specific filings and testimony are the most helpful types of evidence, given the fact-specific nature of each decision. *See Doe v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 328, 338–39 (2007). To that end, experts are an essential piece of a petitioner's claim and Respondent's defense. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at1347 (citing *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000)).

V. Discussion

A. Ms. Delapaz's Diagnosis

Ms. Delapaz was comprehensively evaluated over a course of several years for her varied symptoms. She underwent numerous tests and saw multiple specialists, some of whom diagnosed her with dysautonomia. Dr. Low described dysautonomia as a terrible, vague term. However, both experts as well as Ms. Delapaz's treaters could all agree that she had "something awry with [her] autonomic nervous system." Tr. 213:19–20. Unfortunately, that appears to be the extent of their agreement. Ms. Delapaz was vaccinated on May 15, 2012. As of June 14, 2013, Dr. Butler, her

dysautonomia specialist, noted that he still sought to identify "a complete and appropriate diagnosis in [Ms. Delapaz,] rather than treating her symptoms without a definitive diagnosis." Pet'r's Ex. 5 at 8. Ms. Delapaz was also consistently diagnosed with a neurogenic syncope originating from the nervous system. Her syncope, more commonly known as fainting, was attributed to autonomic dysfunction, medication, or stress and anxiety. Ms. Delapaz's other diagnoses included POTS, CFS, autoimmune dysautonomia, immune-mediated neuropathy, and autoimmune neuropathy. None of these umbrella conditions, which are largely diagnosed through symptomatology after many other causes have been ruled out, are as specific as AAG. Ms. Delapaz's medical records do not indicate that any of her treaters believed that she had AAG. And yet, despite differing opinions from her treaters, Dr. Blitshteyn is confident that Ms. Delapaz suffered from AAG. Dr. Blitshteyn was asked on several occasions to explain why she believes Ms. Delapaz's treaters did not diagnose AAG. She acknowledged that Ms. Delapaz's case is atypical given the lack of antibodies and the presence of sensory symptoms.

The medical record does not provide preponderant evidence that Ms. Delapaz had AAG. Although tested, she lacked the antibody directly related to the disease. Dr. Blitshteyn noted that the antibody is not detected in all patients, but Ms. Delapaz's presentation is too atypical to adopt the diagnosis of a non-treating expert. Indeed, Dr. Blitshteyn testified that the typical AAG patient has widespread autonomic failure affecting all parts of the autonomic system. She asserted that Ms. Delapaz had evidence of anhidrosis, dry mouth, dry eyes, urinary retention, and impaired pupillary light response. She conceded that autonomic function tests did not reveal OH but argued Ms. Delapaz's symptoms of dizziness, lightheadedness, and syncope are evidence of OH. Dr. Low discussed these same symptoms during his testimony. He distinguished Ms. Delapaz's symptoms, including blurry vision, "medication-induced" anhidrosis, and vomiting due to stomach irritation, with symptoms of cholinergic autonomic neuropathy: fixed and dilated pupils, loss of sweat, and gastroparesis. Tr. 219–222. Dr. Low also contested Dr. Blitshteyn's assertion that Ms. Delapaz exhibited signs of OH, given her normal results on two tilt table tests. Dr. Low did not deny that Ms. Delapaz's results on his own CASS reveal some level of autonomic dysfunction. However, his concerns that her medication compromised her QSART test, along with her lack of antibodies and symptomology, cemented his belief that she did not suffer from AAG specifically. The severe disabling nature of Ms. Delapaz's case also helped to convince Dr. Blitshteyn that Ms. Delapaz suffered from seronegative AAG. Dr. Low disagreed and testified that "incapacity and the great effect it has on quality of life, while it[is] terrible, are not symptoms of AAG." Tr. 279:9–11.

It is common in the Program for opposing experts to disagree on the relevant disease or disorder. In this case, that disagreement is of particular significance because Dr. Low is the undisputed expert in AAG. Even Dr. Blitshteyn stated at times during her testimony that she would have to defer to him. Dr. Low did not dispute the evidence that Ms. Delapaz suffered from some sort of condition that negatively impacted her autonomic system. However, he provided alternative causation for her symptoms. I am not a doctor, and I will not get into the business of dissecting and splicing medical records, literature, and expert opinions to diagnose Ms. Delapaz when so many that are qualified could not. Petitioner has alleged that Ms. Delapaz suffered from AAG as a result of her HPV vaccination. For Petitioner's claim to be successful, she must establish it more likely than not that Ms. Delapaz suffered from the condition alleged. In the face of Dr. Low's testimony and the opinions of her actual treaters, I do not find that Petitioner has established it more likely than not that Ms. Delapaz had AAG.

B. *Althen* Prong One

Although Petitioner has not established by preponderant evidence that Ms. Delapaz suffered from AAG, Dr. Blitshteyn focused her theory on AAG. Drs. Blitshteyn and Low agree that molecular mimicry is a viable biological mechanism to explain the development of AAG, but they disagree that the HPV vaccine can be the trigger. Molecular mimicry is a biological mechanism that is often presented in the Program, but its applicability in non-Table cases is often highly disputed. Many of the injuries that are asserted are so rare that scientists and/or physicians are unable to devise, fund, or execute studies to identify the cross-reacting antigens that could be involved in a molecular mimicry pathogenesis. In the case of AAG, not only has the study been done, but the researching physician testified in the case. Dr. Low described how his team "identified the target, and [] specified what the antigen is, it[is] Alpha 3 acetylcholine receptor." Tr. 259:12–13. Dr. Low also noted that his team tested for cross-reactions with the entire range of Alpha antibodies but could not reproduce the disease with any other Alpha subunit. Dr. Low gave a clear description of the process of elimination for other potential cross-reaction sites for AAG. Based on his research and discovery, Dr. Low reasoned that because the HPV vaccine does not contain the Alpha 3 receptor, there could be no such cross-reaction. He further testified that there is no evidence that links the HPV vaccine to AAG.

Dr. Blitshteyn largely relied on Dr. Low's AAG research to form her opinions. She testified that she would have to defer to his testimony on multiple occasions. She further agreed that the AChR "transmits all of the signals in the autonomic nervous system," with a signal block resulting in significant system failure. Tr. 89. Dr. Blitshteyn did not rebut Dr. Low's testimony that his team tested other Alpha subunits for a potential cross reaction. She did not assert that the Alpha 3 receptor is in the HPV vaccine. Instead, she asserted that there may be other, yet unidentified proteins that can also cross-react to cause AAG.

Although identifying a specific antigen is not needed for a claim to be successful, attributing a pathogenic cross-reaction to some unidentified protein is speculative without some supportive evidence. I must note this evidence does not have to take the form of homology. For instance, Dr. Low's discovery with respect to AChR is not based on a BLAST search for homologous peptide chains. Indeed, there is no exhaustive list of what qualifies for supporting evidence of molecular mimicry. Case law tells us what has been previously useful, including acceptance of the theory in a minority population of the medical community, epidemiological studies, expert's experience, and published medical literature. *See Pafford*, 2004 WL 1717359, at *4 (internal citations omitted). I must explicitly state, however, that none of these types of evidence, individually or in tandem, are necessary. They are listed only to illustrate some examples of the kind of evidence used to apply the general molecular theory to a specific alleged vaccine-caused injury. While molecular mimicry may constitute a reliable causation theory involving the flu vaccine and GBS for example, that fact does not render it a persuasive theory when evaluating every and any autoimmune disease following every and any vaccination. *See McKown v. Sec'y of Health & Hum. Servs.*, No. 15-1541V, 2019 WL 4072113 at *50 (Fed. Cl. Spec. Mstr. July 15, 2019) ("[M]erely chanting the magic words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent additional evidence specifically tying the mechanism to the injury and/or vaccine in question.").

Dr. Blitshteyn relied on case reports of autonomic disorder following HPV vaccination to show a pattern of cases with similar symptoms to the alleged injury in this case. Indeed, an article that she published (and filed) suggests that several other autoantibodies (and therefore molecular mimicry) have been associated with autonomic disease. *See* Pet'r's Ex. 42 (finding a case of POTS associated with anti-NMDA antibodies post HPV vaccination). Notably, none of these filings, including hers, mentions AAG. They focus on POTS, and to a lesser degree, CRPS.[92] Dr. Blitshteyn did not contend that this claim involves POTS, but she argued that AAG and POTS are similar enough for analogy. While the symptomology may be related in these conditions, Dr. Blitshteyn did not present supporting evidence that analogizes the etiology of POTS to AAG. Furthermore, Dr. Blitshteyn did not reveal a link in Dr. Low's research between POTS and AChR.

In an article filed by Petitioner, Dr. Low does identify POTS as a "clinical phenotype of AAG." Pet'r's Ex. 33 at 4. Dr. Low's concession that AAG may present as POTS was clarified by Dr. Low during his testimony, albeit in a manner described even by him as "a bit contradictory." Tr. 300:24. He asserted that there is no "compelling evidence" that POTS is fundamentally immunologic. Tr. 300:22–23. He then explained that the syndrome is indicative of an immunologic disorder only when it is secondary to, or when it is a clinical manifestation of, a known immunologic disease. *See* Tr. 301. The first Chustecka article supports Dr. Low's position. *See* Pet'r's Ex. 43 at 1. Chustecka discussed one report, published in the *Danish Medical Journal,* that warns "POTS should probably be looked upon as a symptom secondary to another yet unidentified condition rather than as a disease entity of its own." *Id.* at 2. This reasoning effectively differentiates POTS, a syndrome defined largely by symptoms on a spectrum, from AAG, a disease that is defined by a targeted neuropathy. The evidence shows that POTS may overlap with AAG in terms of orthostatic symptoms. However, Petitioner has not presented persuasive evidence explaining why the literature suggesting a link between HPV and POTS also supports a similar etiology for AAG.

Dr. Blitshteyn's theory is further complicated by the incorporation of an acute aluminum allergic reaction into the immune process that initiates the molecular mimicry. During her testimony, Dr. Blitshteyn was asked how Gardasil caused AAG. She first testified that there was an IgE-mediated reaction that helps her "put this together." Tr. 123:15. She then said that aluminum salt, a component of the vaccine's adjuvant, triggered a T helper 2 immune response and a non-IgE mediated allergic reaction. Tr. 123:18–23. She did not say if the T helper 2 response and the non-IgE mediated response were intertwined, counteractive, or independent occurrences. A Medscape article filed by Dr. Blitshteyn offers support that "non-mediated-IgE mast cell and basophil degranulation" can result from substance triggers, such as opiates. Pet'r's Ex. 31 at 2. Dr. Blitshteyn argued that this process that causes the release of histamine and tryptase can also be triggered by aluminum. She did not provide any literature in support of this argument. She then pivoted to the Th2 response, stating that it leads to the activation of B cells and the production of antibodies, antibody cross-reaction, and ultimately the onset of AAG. Tr. 185:9–13. When asked how cellular degradation that occurs during a non-antibody-mediated reaction leads to AAG, an antibody-mediated disease characterized by the impairment of synaptic transmission in autonomic ganglia, she responded "that[is] the million dollar question." Tr. 186:6.

[92] CRPS is not an autonomic disease, and Dr. Blitshteyn did not assert that a molecular mimicry pathogenesis for AAG can be derived from studies of CRPS following a Gardasil vaccination.

She reiterated that it was the aluminum and not vaccine protein sequences that caused an allergic reaction. Given Dr. Blitshteyn's description of an autoimmune autonomic syndrome induced by an aluminum adjuvant, I asked her about ASIA. She testified that she has limited familiarity with ASIA and that she has "not reviewed one paper with ASIA for this case." Tr. 189:22–190:2. However, Petitioner filed an article by Palmieri et al. that expressly lists ASIA as a keyword. Pet'r's Ex. 41 at 1. ASIA is mentioned twenty-four times in this exhibit, not including the references. The paper's abstract describes a case series of girls evaluated for neuropathy with autonomic dysfunction after HPV vaccination and states, "[t]hese cases can be included in the recently described immune dysfunction named autoimmune/inflammatory syndrome induced by adjuvants (ASIA)." *Id.* at 1. The authors opined that "all these heterogeneous post-vaccination phenomena might be the consequence of some immune dysfunction, putatively activated by the adjuvant rather than by antigenic vaccine fractions." *Id.* at 5. It is difficult to see a distinction between the authors' hypothesis and Dr. Blitshteyn's theory. Given the string of unsuccessful cases that have identified ASIA as the likely biological mechanism, there is good reason for Dr. Blitshteyn to try to distinguish her theory. *See D'Angiolini v. Sec'y of Health & Hum. Servs.*, 122 Fed. Cl. 86, 102 (2015) (upholding special master's "determin[ation] that ASIA does not provide[] a biologically plausible theory for recovery"), *aff'd*, 645 Fed. Appx. 1002 (Fed. Cir. 2016); *Garner v. Sec'y of Health & Hum. Servs.*, No. 15–063V, 2017 WL 1713184, at *8 (Fed. Cl. Spec. Mstr. Mar. 24, 2017) (observing that the ASIA theory "is, at a minimum, incomplete and preliminary—and therefore unreliable from an evidentiary standpoint"); *Rowan v. Sec'y of Health & Hum. Servs.*, No. 10–272V, 2014 WL 7465661, at *12 (Fed. Cl. Spec. Mstr. Dec. 8, 2014) (rejecting the ASIA theory because it "is not a proven theory" and no "persuasive or reliable evidence" supports it); *Johnson v. Sec'y of Health & Hum. Servs.*, No. 10–578V, 2016 WL 4917548, at *7–9 (Fed. Cl. Spec. Mstr. Aug. 18, 2016) (rejecting a theory that "any adjuvant [is] capable of causing any autoimmune disease," finding it "overbroad, generalized, and vague, to the point that it could apply to virtually everyone in the world who received a vaccine containing an adjuvant and then at some time in their lives developed an autoimmune disease"). However, it strains credibility that the theory in this case is not at least partially, based on ASIA. Setting aside any resemblance to ASIA, Dr. Blitshteyn was unable to say how her theory incorporates the HPV vaccine or AAG, specifically. She was unable to explain her basis for asserting that the aluminum adjuvant in the vaccine contains an antigen capable of cross-reacting to induce AAG. She was unable to say if any adjuvanted vaccine would have caused this injury. She was unable to describe how an aluminum adjuvant can induce a non-IgE mediated reaction to initiate the entire process.

Dr. Blitshteyn's testimony that an aluminum allergy is not the cause here muddles the theory even more. She described a reaction "to salts by histamine release from mast cells, not from antibodies." Tr. 187:21–22. Her assertion that there is a histamine release that is not caused by antibodies in an antibody-mediated disease is not persuasive. Ultimately, her theory is convoluted and speculative. After considering all the evidence and testimony that Petitioner presented in this case, I find that she has not presented preponderant evidence that the aluminum adjuvant, nor any other component of the HPV vaccine, can incite a non-IgE mediated reaction and/or a Th2 reaction that, through molecular mimicry, causes AAG or Ms. Delapaz's condition. Petitioner has not met her burden with respect to prong one.

C. *Althen* Prong Two

Petitioner did not provide preponderant evidence of how HPV vaccination can cause AAG. She also did not establish with preponderant evidence that Ms. Delapaz suffered from AAG. It is therefore difficult to determine if the vaccine is the cause of Ms. Delapaz's symptoms. In order to show how to apply her asserted theory to Ms. Delapaz, Dr. Blitshteyn analogized the symptomology and pathology of POTS to AAG. She then relied on medical literature and her own experience to assert that like instances of POTS, Ms. Delapaz's condition was similarly caused by the HPV vaccine. This analogy is less helpful, given that claims of POTS following an HPV vaccine have not been successful in the Program. *See, e.g.*, *America v. Sec'y of Health & Hum. Servs.*, No. 17-542V, 2022 WL 278151, at *27 (Fed. Cl. Spec. Mstr. Jan. 4, 2022) (ruling against Petitioner's argument that the HPV vaccine can interfere with the nervous system sufficient to cause POTS, autonomic dysfunction or generalized dysautonomia, or vasovagal syncope); *Hughes v. Sec'y of Health & Hum. Servs.,* No. 16-930V, 2021 WL 839092, at *30 (Fed. Cl. Spec. Mstr. Jan. 4, 2021) (denying compensation for a claim involving the HPV vaccine and POTS); *E.S. v. Sec'y of Health & Hum. Servs.,* No. 17-480V, 2020 WL 9076620, at *49–51 (Fed. Cl. Spec. Mstr. Nov. 13, 2020); *Balasco v. Sec'y of Health & Hum. Servs.,* No. 17-215V, 2020 WL 1240917, at *33–34 (Fed. Cl. Spec. Mstr. Feb. 14, 2020); *Yalacki v. Sec'y of Health & Hum. Servs.,* No. 14-278V, 2019 WL 1061429, at *34 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *review denied*, *aff'd.* 146 Fed. Cl. 80 (2019) (finding that the evidence presented to show POTS is autoimmune was thin and that Petitioner failed to show an HPV vaccine likely causes "the production of antibodies associated with autonomic damage or interference sufficient to cause POTS"); *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *1 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (ruling against Petitioner in a case alleging that the HPV vaccine caused POTS and noting that the medical literature suggesting that POTS "might be autoimmune appears [to be] extremely limited"); *L.A.M. v. Sec'y of Health & Hum. Servs.,* No. 11-852V, 2017 WL 527576, at *63 (Fed. Cl. Spec. Mstr. Jan. 31, 2017) (finding that most cases of POTS do not have an autoimmune etiology and that Petitioner's claim that the HPV vaccine caused POTS must fail because she did not provide corroborating evidence of an autoimmune process); *Combs v. Sec'y of Health & Hum. Servs.*, No. 14-878V, 2018 WL 1581672 (Fed. Cl. Spec. Mstr. Jan. 31, 2017).

Dr. Low maintained during his testimony that a conversation on POTS was irrelevant to the facts in this case because AAG and POTS are not related. This assertion is belied by Dr. Low's own writings that were filed by Petitioner. His explanation that POTS is not relevant because it is not immune-mediated does not address his own prior opinion that POTS is a clinical phenotype of AAG. His inconsistency on this point renders useless his assertion that consideration of POTS is unhelpful. Assuming that POTS is relevant to the presentation of AAG, however, Dr. Blitshteyn undercut the importance of this point. She likened Ms. Delapaz's condition not to the POTS phenotype but to another phenotype described by Dr. Low as limited or continued autonomic dysfunction, including gastrointestinal issues or cholinergic autonomic failure. Gastrointestinal issues, while seen in Ms. Delapaz's case, are not characteristic of POTS. The differences between POTS and Ms. Delapaz's orthostatic symptoms are also revealed in the lack of intolerance detected during her tilt table tests. Even stripping away the details of Dr. Blitshteyn 's biological mechanism and the specific name of Ms. Delapaz's disease, I am unable to see preponderant evidence that the vaccine played a role in her continued symptoms.

The record does reflect preponderant evidence that Ms. Delapaz suffered from an acute reaction to the HPV vaccine. Her treaters indicated on multiple occasions that this allergic reaction resolved shortly after onset. The medical record indicated that Ms. Delapaz experienced chest pain, wheezing, and headache the same day as her vaccination. These symptoms were accompanied by injection site swelling, and she was diagnosed with an allergic reaction. Two months post vaccination, Ms. Delapaz was seen by her allergist with no complaints of chest tightness, dizziness, headache, or any number of other symptoms commonly associated with allergies. While Ms. Delapaz later experienced allergic reactions to other substances such as pineapple and cologne, there is no evidence to tie these reactions back to her May 15, 2012 vaccination.

In August, Petitioner reported to Ms. Delapaz's treater that she had a long history of intermittent allergic episodes. Pet'r's Ex. 25 at 156. Indeed, Ms. Delapaz's medical record includes a significant history of various allergies and asthma, many of which predate her HPV vaccination. I do not find there is preponderant evidence that her acute allergic reaction to the vaccine meets the durational or severity requirement for entitlement in the Program. *See* § 11(c)(1)(D). Specifically, while Ms. Delapaz did suffer an allergic reaction to the HPV vaccine, this injury did not last six months, result in death, or require surgical intervention. Furthermore, as noted in the prong one discussion, Dr. Blitshteyn did not offer preponderant evidence of a theory that links an acute allergic reaction to HPV to the development of antibody-mediated AAG. Therefore, I could not identify such a logical sequence of cause and effect in Ms. Delapaz's case. Petitioner has not met her burden pursuant to prong two.

D. *Althen* Prong Three

Finally, Petitioner is tasked with establishing by preponderant evidence that there is an appropriate temporal relationship between vaccination date and the onset of injury that is incorporated into the offered biological mechanism and applicable to the facts in the present case. This prong is especially difficult to evaluate because Dr. Blitshteyn was unable to answer clarifying questions concerning timing and onset. In her report, Dr. Blitshteyn stated that the appropriate onset for AAG following cross-reaction of autoantibodies is within four weeks. Pet'r's Ex. 50 at 4. She testified that Ms. Delapaz's initial immune response began within hours of her vaccination. Tr. 172:7–9. She later added that "it will be a guessing game for [her] when there is an end to the allergic process," which triggered the autoimmune reaction. Tr. 186:6. Because Dr. Blitshteyn conflated the timing of the allergic reaction with the onset of AAG, she is less helpful on this point. Alternatively, Dr. Low testified that AAG is not the result of acute mediators. He described onset as a "delayed response" of one to six weeks. Tr. 252:2–5. I will use this temporal relationship in my analysis of Ms. Delapaz's medical records.

Dr. Blitshteyn identified headache, dizziness, and weakness as evidence of continued autonomic symptoms within three weeks following vaccination. These symptoms all appear in a May 4, 2011 medical record, one full year prior to vaccination, where Ms. Delapaz complains of headache, dizziness and fatigue. Pet'r's Ex. 21 at 495. There is also a complaint of constipation, a gastrointestinal symptom. These symptoms appear again throughout Ms. Delapaz's post vaccination medical record, along with her complaints of allergic reactions. Although these symptoms are potentially indicative of autonomic dysfunction, they can also be fairly nonspecific.

It is difficult to assign them weight as a definite marker of dysautonomia onset, pre or post vaccination.

Dr. Low identified dilated pupils during a hospitalization in November of 2012, as the first possible autonomic symptom in Ms. Delapaz's medical record. He noted that the examining physician at that time diagnosed her with sympathetic overactivity. *See* Tr. 252. Dr. Low asserted that Dr. Rotenberg's note of a four-month history of numerous idiopathic autonomic symptoms referred to instability in heart rate and blood pressure, not signs of autonomic damage. Dr. Low could not point to any possible symptoms of autonomic damage that occurred within six weeks of Ms. Delapaz's vaccination, that did not also occur pre-vaccination. I agree. Petitioner has not presented preponderant evidence that Ms. Delapaz's onset of symptoms has an appropriate temporal relationship with her HPV vaccine to be indicative of causation. Petitioner has not met her burden pursuant to prong three.

VI. Conclusion

After a careful review of the record, Petitioner has failed to prove by preponderant evidence that Ms. Delapaz suffered from AAG and that her condition was caused-in-fact by her May 15, 2012 HPV vaccination. Accordingly, I have no choice but to **DENY** Petitioner's claim and **DISMISS** her petition.[93]

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master

[93] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.